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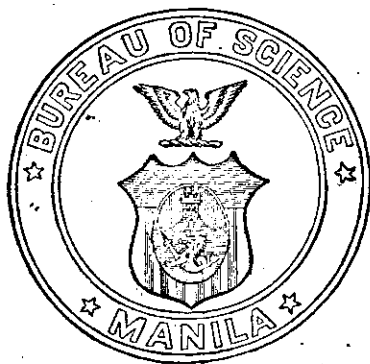
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CIRCULARS AND DESCRIPTIVE MATTER SENT ON APPLICATION.

# THE PHILIPPINE JOURNAL OF SCIENCE

B. MEDICAL SCIENCES

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## DAVAINEA MADAGASCARIENSIS (DAVAINE) IN THE PHILIPPINE ISLANDS.

By PHILIP E. GARRISON.<sup>1</sup>

The worms studied in the present paper were received from Dr. Vernon L. Andrews, of the department of bacteriology and pathology of the College of Medicine and Surgery, University of the Philippines, who collected them at autopsy from the small intestine of an adult, male Filipino, at the morgue in Manila in March, 1909. Doctor Andrews's specimens are of particular interest because the last finding of *Davainea madagascariensis* (Davaïne) was fourteen years ago, and this is only the sixth which has been reported. Infection with this species has been observed only ten times, and the occurrence which forms the subject of this paper marks the Philippines as a new locality in the interesting geographical distribution of this parasite. This new material offers an opportunity for a further study of the anatomical characters of the species.<sup>2</sup>

### HISTORY OF THE SPECIES.

In 1867, Dr. Grenet obtained the first specimen from a male child eighteen months old, at Mayotte, Comoro Islands. This child had landed five months before from the Antilles. Later, Dr. Grenet secured a second specimen from a girl two years old, native of Reunion Island, who had been in Mayotte

<sup>1</sup>Passed assistant surgeon, United States Navy, formerly detailed medical zoölogist for the Bureau of Science, Manila.

<sup>2</sup>I am indebted to Dr. Ch. Wardell Stiles for access to a part of the original papers consulted, and to Dr. Brayton H. Ranson for several suggestions regarding the interpretation of certain anatomical characters.

two months. Only about fifteen isolated terminal segments of the worm were secured from the first case. The second specimen consisted apparently of a fairly complete strobila, but was without a head. These specimens were sent to the Directeur des Archives de Medicine and forwarded to Davaine, who, in 1869, described and figured the worms and proposed a new species which he called *Tania madagascariensis*. These specimens were later deposited in the collection of Blanchard's laboratory (Nos. 108 and 109, Collection Davaine).

In 1873, a second finding of the species was made at the small island of Nosse-Bé, just off the northwest coast of Madagascar. This was not published until 1899 when Blanchard found the specimen in the parasite collection of the Faculty of Medicine of Paris (No. 33, Collection Davaine) bearing the label "Nosse-Bé, November, 1873, passed by a little girl of three years." This specimen was very incomplete, being only 32 millimeters long, but it possessed the head, and Blanchard's paper in 1899 gave the first description and the only published drawing of the head of this species.

In April, 1891, Dr. P. Chevreau announced the finding of four cases of infection with *D. madagascariensis* in children at Port Louis, on Mauritius Island, off the west coast of Madagascar, where, at the instigation of Blanchard, he had made a special search for the parasite. Two of the children were little girls of five years. The sex and age of the other two were not given. The specimen from one of the children, which was sent to Blanchard (Collection R. Blanchard, No. 8) consisted originally of three fragments which in transit were broken into eight, and, according to Blanchard, represented parts of two worms. There was no head. Blanchard gave a brief description of the specimen in 1891.

In the same year (1891) Leuckart reported that he had received from Krabbe a specimen of *Davainea madagascariensis* collected at Bangkok, Siam, from the three-year-old son of a Danish sea captain, living on his father's ship which was plying in Asiatic waters. Later in 1891, Leuckart reported the results of his study of the specimen, which consisted of a single worm about 24 centimeters long, including the head. This material was further studied by Holzberg in 1897.

The fifth and last finding of the species prior to the present one was reported from South America in 1895 by Daniels who obtained two specimens at autopsy from the jejunum of an adult, male aboriginal Indian at Georgetown, British Guiana. The heads were not found and, having only Davaine's original description of *D. madagascariensis* available, Daniels considered his specimens to be specifically distinct and proposed a new species under the name "*Tania demericensis*?" A part of Daniels's material was sent to Sir Patrick Manson and through him reached Blanchard (Collection R. Blanchard, No. 236) who established its identity with *D. madagascariensis*.

The history of the six findings of *Davainea madagascariensis*, accordingly, extends over a period of forty-two years, and may be summarized as follows:

Grenet, 1867, Comoro Islands, two cases (male child eighteen months old and girl two years old, from the Antilles and from Reunion, respectively), two worms without heads; specimens studied and published with illustrations by Davaine in 1869.

—, 1873, Nosse-Bé Island, one case (three-year-old girl), one immature worm with head; specimen found in Davaine collection, studied and published by Blanchard in 1899 with figure of head.

Chevreau, 1891, Mauritius Island, four cases (two girls five years old, two with age and sex unknown); fragments of two worms without head from one case sent to Blanchard and briefly described the same year.

Krabbe, 1891, Siam, one case (Danish boy three years old); one specimen

complete with head; published by Leuckart in 1891. (Further studied by Holzberg, 1897.)

Daniels, 1895, British Guiana, one case (adult, male native), parts of two worms, no head; published in 1895 as *Tania demerariensis* with illustrations; part restudied and published by Blanchard in 1899.

Andrews, 1909, Manila, P. I., one case (adult, male Filipino), one complete worm and four nearly complete except the head; deposited, No. 305, in Helminthological Collection, Bureau of Science, Manila, and reported in the present paper.\*

Three other papers are of special interest in the history of this species.

In 1891 Blanchard and Railliet established the genus *Davainea* in which they placed about twenty-five species, including *D. madagascariensis*.

In 1896 Stiles established *D. proglottina* (Davaine, 1860) of poultry as the type species of the genus *Davainea*.

In 1898 Holzberg published a careful study of the reproductive organs of the genus *Davainea*, Leuckart's specimen of *D. madagascariensis* being among the material examined.

#### IDENTITY OF THE SPECIMEN.

Certain not insignificant differences between the anatomical structure of the Philippine specimen and that described for earlier specimens of *Davainea madagascariensis* will be noted in the course of the following description. These differences were such that it seemed at first that we must be dealing with another species. Further study of the specimen and a careful comparison in detail with the figures and descriptions of other authors have convinced us that while certain differences exist seemingly scarcely consistent with specific identity, an actual comparison of the different specimens will be necessary before the real value of such variations can be ascertained. Such a comparative study should prove most interesting and valuable as well in clearing up certain anatomical differences apparently existing between the several specimens heretofore described. Until the actual comparison of specimens can be made, there is no doubt that Dr. Andrews's specimens found in the Philippines should be placed with those of Grenet, Chevreau, Krabbe, and Daniels in the species *Davainea madagascariensis* (Davaine, 1869) Blanchard and Railliet, 1891.

#### DESCRIPTION OF SPECIMEN.

The specimens received from Dr. Andrews consisted of five worms, one complete with head and gravid segments, the other four evidently nearly complete excepting the head. The five worms were entered in the Helminthological Collection as number 305, A, B, C, D, E. The specimens were killed in an alcoholic solution of bichloride of mercury and preserved in 70 per cent alcohol containing 5 per cent of glycerine.

The size and general characters are as follows:

305 A.—Thirty-nine centimeters long, head present and strobila complete in one piece from head to gravid segments.

305 B.—Twenty-eight + centimeters long, head and neck missing, remainder of worm in one piece from near the neck to gravid segments.

\*It may be noted that while Davaine named the species after Madagascar, as indicative of the general locality where the first specimens were found, the parasite has never been reported from Madagascar itself.

305 C.—Twenty-nine + centimeters long, head and neck missing, remainder of worm in one piece from near the neck to gravid segments.

305 D.—Twenty-nine + centimeters long, head and neck missing, remainder of worm in one piece from near neck to gravid segments.

305 E.—Four fragments, apparently parts of the same worm; two pieces, 1.5 centimeters and 9 centimeters long, respectively, consisting of rectangular segments; two pieces, 2.5 centimeters and 13 centimeters long, respectively, consisting of terminal, barrel-shaped segments.

The complete specimen with head (305 A) was mounted *in toto*. Specimen 305 D and portions of 305 E were used for sections and digestion. In determining the various anatomical characters, all of the material has been studied.

#### EXTERNAL ANATOMY.

*Head*.—The head and neck unfortunately became badly folded in mounting. The actual breadth of the head as it lies is  $256\ \mu$ . Allowing for the folding, its full breadth appears to be about  $320\ \mu$  but certainly can not exceed  $400\ \mu$ . Blanchard described the head as about  $930\ \mu$  broad by  $510\ \mu$  long.

Leuckart does not give the general dimensions.

The *suckers* in their greatest diameter measure from  $105$  to  $125\ \mu$ , their lumina from  $30$  to  $45\ \mu$ . They are devoid of hooks. In Blanchard's specimen the suckers measured  $465\ \mu$  in diameter with a lumen  $100\ \mu$  in diameter. They also were unarmed. Leuckart does not mention the presence of hooks on the suckers of his specimen.

The *rostellum* is strongly retracted within the head and its contour can not be made out. Imbedded in the head there remain about twelve hooks of the rostellum, of the peculiar "hammer-like" shape of *Davainea*. These hooks measure  $23.5$  to  $25.2\ \mu$  long over all. The long root is rather sharply bent somewhat beyond its middle and measures about  $21\ \mu$  in length and is about  $5.6\ \mu$  broad as it joins the blade. The blade and the short root are continuous in one line, each projecting about  $2.8\ \mu$ , the blade being sharply curved and the short root straight and blunt.

In Blanchard's specimen the rostellum was invaginated, forming an apical sucker  $250\ \mu$  in its transverse diameter and  $145\ \mu$  deep with a deep cup-like depression  $83\ \mu$  in its greatest (transverse) diameter. The hooks were absent, having evidently fallen off. In Leuckart's specimen the rostellum was plump, retracted, about  $100\ \mu$  broad and presented a circular depression at the apex of the head. Around the equator of the rostellum was a ring of about 90 peculiarly shaped hooks, each with a long, slightly curved root measuring  $18\ \mu$ , a short, blunt, posterior root, and a blade about one-eighth the length of the long root, with which it makes an angle of about  $70^\circ$ .

*Neck*.—Because of the folding of the specimen the real breadth of the neck can not be made out with entire satisfaction, but it appears to be about the same as the head, and it is not possible to make out any tendency to the broadening of the neck behind the suckers as described by Blanchard. From behind the suckers the neck gradually grows narrower and reaches a minimum breadth of about  $160\ \mu$  at a distance of about 2 millimeters from the tip of the head. At about this same point the first signs of segmentation are seen and the genital primordia appear shortly after.

Leuckart states that the breadth was "only  $500\ \mu$  just behind the head." Blanchard's specimen measured  $1,240\ \mu$  a short distance behind the head and then decreased to a minimum of  $500\ \mu$ , at which point segments are already defined.

*Segments*.—As stated, segmentation appears at about the minimum breadth of the worm ( $160\ \mu$ ) at a distance from the tip of the head of about 2 milli-

meters. The youngest segments are only about  $50\ \mu$  long, there being about 20 in the first millimeter after their appearance. Gradually increasing in length and breadth the segments attain a maximum breadth of 1.5 millimeters about 15 centimeters from the tip of the head and at this place the length of the segments has increased to something less than 1 millimeter, 1 centimeter of the length of the strobila containing from twelve to fifteen segments. Thereafter, the segments increase in length, remaining about the same in breadth, for a distance of from 10 to 12 centimeters, when they are about square. The lengthening then continues, while the breadth shows a tendency to decrease, the segments at the same time beginning to take on the "barrel" shape which becomes more pronounced as we approach the posterior extremity. The terminal gravid segments, which comprise some 10 to 12 centimeters of the length of the strobila, measure about 2 to 2.5 millimeters long by 1 to 1.5 millimeters broad.

The total number of segments in specimen 305 A is about 600.

The younger segments tend to a trapezoidal form, the posterior border being somewhat broader than the anterior and overlapping the anterior extremity of the succeeding segment.

The genital pores are not prominent and in the younger segments are situated near the cephalic extremity of the lateral border, later holding a more posterior position, but always well forward of the mid-plane of the segments. They are unilateral with occasional transpositions. Usually the pore will be found on the opposite side in only a single segment, occasionally in two or three, and in one case (specimen 305 D) the pore was found transposed in about 70 consecutive segments.

#### INTERNAL ANATOMY.

*Excretory canals.*—The ventral excretory canals can be followed throughout the length of the strobila, connected at the posterior border of each segment by a transverse canal and attaining maximum diameters of 40 by  $20\ \mu$ . The dorsal canal is about half the size of the ventral and can be followed in sections almost throughout the strobila. It is placed in a plane considerably mediad to that of the ventral canal, and both canals are situated a considerable distance to the median side of the lateral nerve. The vagina and vas deferens pass between the two canals and behind the lateral nerve in all the segments in which the relative position could be determined.

*Genital organs.*—As indicated above, the segments develop sexually very early in the strobila, the primordia of the genitalia appearing as a dark line in the median field almost with the first appearance of segmentation and while the segments are still only about 160 by  $50\ \mu$  and about 2.5 millimeters from the tip of the head.

The testicles appear early, when the segment is scarcely  $500\ \mu$  broad and  $200\ \mu$  long, and before the female genital glands have been clearly differentiated. They are about 50 in number, scattered through the parenchymatous tissue, internal to the excretory canals, and are roughly divided into a dorsal and a ventral layer. The vas deferens is extremely long and coiled, extending from the cirrus pouch to about the median line, the coils filling an area from 60 to  $120\ \mu$  broad. The cirrus pouch is distinctly bottle- or gourd-shaped, situated in the antero-lateral corner of the segment, with its long diameter (neck) directed outward and backward. It measures from 120 to  $160\ \mu$  in length by 64 to  $100\ \mu$  in breadth. The narrowed neck of the pouch may be nearly straight but more frequently is curved like the neck of a gourd, its concavity being posterior.

After entering the pouch the vas deferens makes two or three irregular coils and enters the cirrus, which is about  $80\ \mu$  long with a maximum breadth of

12.8  $\mu$ . The *cirrus* is found retracted in most segments, but in a few it is extruded beyond the margin of the segment to a distance of about 25  $\mu$ , the extruded portion being about 8  $\mu$  broad at its base and tapering.

The *vagina* opens immediately posterior to the male orifice, into the common genital *cloaca*, which is rather shallow and projects at the most but a few (15 to 20)  $\mu$  beyond the lateral line of the segment. Close to its outer extremity the vagina presents a well-marked dilatation, the *receptaculum seminis*, which measures 60  $\mu$  long, and 28  $\mu$  broad, being only about one-half the length of the *cirrus* pouch and reaching not one-half the distance from the lateral border to the ventral excretory canal, whereas, in Krabbe's specimen, according to both Leuckart's description and Holzberg's drawing, the *receptaculum seminis* extended nearly the entire length of the vagina, reaching nearly or quite to the median line of the segment.

From the dilated portion, the *vagina* pursues a course inward and slightly caudad to the median line, where it turns sharply caudad to join with the oviduct, the conjoined tube becoming surrounded by the *shell gland*, and receiving the duct from the *yolk gland* to form the *ootype*. The *uterus*, so far as its structure can be made out in the sexually active segments, appears to consist of a median cavity composed of a number of pouches. The exact arrangement of these pouches and the manner of their gradual extension throughout the segment could not be determined clearly in the sections made, but it seems that the primitive uterine structure gradually extends outward through the parenchymatous tissue of the segment, dividing and subdividing as it progresses, and that small portions, containing one, two, or three eggs each, then become constricted off and lie encased in the parenchyma. The egg-balls form around these pinched-off portions, and their inner, granular zone immediately surrounding the eggs would seem to represent the original uterine structure.

The following description of the *eggs* and *egg-balls* is based upon a study of material digested in a solution of hydrochloric acid and pepsin. Both the egg-balls and the eggs themselves presented a very different and undoubtedly a much more natural appearance when so treated than when dehydrated, stained, cleared, and mounted. In the segments mounted in balsam, either *in toto* or in sections, the balls themselves are shrunken, the outer, lighter zone blends with the surrounding tissue and is not clearly distinguished, the outer shell is marked only by the light area immediately surrounding the embryo and the inner shell is shrunken close around the onchosphere.

In the digested segments the *egg-balls* become separated at what appear to be natural lines of demarcation between their own structure and that of the surrounding parenchyma. The individual egg-balls thus set free are round to ovoid and vary considerably in size, measuring from 200 to nearly 400  $\mu$  in diameter. They present a clear, comparatively structureless outer zone and an inner, denser and more darkly staining area, the latter containing the eggs, which may be one, two, or three in number, most often two. Numerous small (8  $\mu$ ) calcareous corpuscles appear within the inner and outer zones.

If digestion is allowed to proceed further, the egg-balls themselves are broken up and the individual *eggs* are set free. The six-hooked onchosphere is inclosed within two envelopes. The outer envelope is extremely thin and delicate and is easily broken up by slight pressure on the cover glass or removed by a little longer digestion. It tapers to a rather sharp extremity at each end and measures about 120  $\mu$  in length by about 48  $\mu$  in breadth. The inner shell is rather thin and easily distorted and broken, but is considerably thicker and stouter than the outer shell. It is nearly colorless, but has a light yellowish-brown tint.

It is very much elongated, measuring from 50 to 64  $\mu$  long by 19 to 23  $\mu$  broad. One end is bluntly rounded, the other rather more tapering.

The *onchosphere* is circular or nearly so and measures 14 to 15  $\mu$  in diameter. On one side is a slight, blunt, flat-topped eminence bearing the three pairs of nearly straight hooklets, the latter being from 4 to 5  $\mu$  long. Usually the *onchosphere* lies near the middle of the long diameter of the egg, but it is occasionally displaced to a position near one end.

Other authors who have studied the egg of *Davainea madagascariensis* (Davaine, Leuckart) describe the inner shell as closely enveloping the embryo. Such would be the interpretation in the present case from the appearance of the egg in the mounted specimens, but from a study of the eggs in digested segments it seems quite clear that the inner shell is normally of the form described above and pictured in figure 4.

#### SIGNIFICANCE OF THE PRESENT FINDING.

The first three findings of *D. madagascariensis* in the islands off Madagascar (in 1867, 1873, and 1891) might well have been taken to indicate a possibly narrow range of distribution in that locality, although one of Grenet's cases had come from the Antilles five months previously. Krabbe's case at Bangkok in 1891 at once widened this range greatly and suggested the possibility of a rather extensive distribution. Daniels's case in British Guiana in 1895, as pointed out by Blanchard, opened a new era in the history of the parasite and indicated a general distribution of the species throughout the Tropics. Still, after a lapse of fourteen years, the parasite was not again encountered until Andrews's case in the Philippine Islands completed the belt of distribution around the world and practically gave final proof of the more or less general tropical distribution of the parasite.

From the viewpoint of age distribution it is noteworthy that while six of the eight cases reported in the first four findings of *D. madagascariensis* were young children, the age of the other two not being stated, the last two cases (Daniels's and Andrews's) were adults.

Another interesting point is the apparent relation between the incidence of the infection and maritime surroundings. The first seven cases were insular and all ten have been found at port towns. In addition, two of Chevreau's patients had arrived by ship two months and five months previously, and Krabbe's case, the son of a sea captain, was said to dwell on his father's vessel. The significance of this seeming relationship is problematical. It might mean that the intermediate host is some animal of wide distribution in the Tropics and particularly infesting such situations as ships and docks, for example, the cockroach (*Periplaneta orientalis*) as Blanchard has suggested. On the other hand, further investigation may show the parasite to exist in the interior as well. Heretofore, there has been comparatively little opportunity for investigation in such regions. If this were the case, the apparent relation between the infection and shipping would, in part at least, lose

its significance. We are not aware of the previous occupation of the individual in whom Andrews encountered the parasite, but his residence in Manila could scarcely fail to afford opportunity for infection about the ships and docks of the harbor and river, if such situations are the home of the intermediate host of the cestode. However, the Manila case taken alone would seem to lend itself to almost any hypothesis regarding the source of infection, whether the intermediate host be an insect, mollusk, or fish; and, when taken together with our knowledge of the earlier cases, the fact that Manila is a seaport with a harbor and river full of docks and shipping surely strengthens rather than weakens the apparent relations which have been noted between infection with *D. madagascariensis* and maritime surroundings.

So far as we are aware no one has suggested any more plausible theory regarding the source of infection with this cestode than that of Blanchard, namely, that the intermediate host of the parasite is probably some animal of general tropical distribution particularly infesting ships and docks, and that the cockroach (*Periplaneta orientalis*) would fulfill these conditions. This theory is based in part, of course, upon the analogy presented by the known life cycles of other species of *Davainea*, the larval forms of which live in arthropods or mollusks.

The question as to whether *D. madagascariensis* is normally parasitic in man, or is accidental, having as its normal host some other animal, is naturally suggested by its comparatively rare occurrence in man and by the further fact that species of *Davainea* are so common in birds and so rare in other animals that it is considered distinctly a bird genus among parasites. But in 1899 Blanchard pointed out that while the great majority of species of this genus were parasites of birds, some five species were then known to be parasitic in mammals,<sup>4</sup> namely, three in rodents, one in the ant eater, and one in man, and he unhesitatingly expressed his opinion that *D. madagascariensis* was a normal and not an accidental parasite of man. That the species has now been found in man ten times and has not been reported from any other host during a period of over forty years of active helminthological research would seem to render it reasonably certain that we have in *Davainea madagascariensis* a parasite normal, and perhaps peculiar, to the genus *Homo*.

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<sup>4</sup>Dr. Ransom informs me that one or two of the mammalian species quoted by Blanchard are probably not true *Davaineas*, but that a number of new species of *Davainea* in mammals have since been reported.

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## ILLUSTRATION.

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Explanation of plate. Figures 1 and 2 were drawn from mounted specimens stained with hydrochloric-acid carmine according to the usual method. Figures 3 and 4 were drawn from digested material lightly tinted with carmine.

The drawings were made by Hospital Apprentice L. Avery, United States Navy.

### PLATE I.

- FIG. 1. Sexually mature segment showing the genital organs.  $\times$  about 40. c.=cirrus; c. p.=cirrus pouch; d. c.=dorsal excretory canal; g. p.=genital pore; l. n.=lateral nerve; ov.=ovaries; t.=testicles; trs. c.=transverse excretory canal; v. c.=ventral excretory canal; v. d.=vas deferens; vag.=vagina; y. g.=yolk gland.
2. Terminal gravid segment, showing egg-balls containing one, two, and three eggs.  $\times$  about 35.
3. Egg-ball from digested segment, showing outer and inner layers, calcareous corpuscles, and two eggs with their double envelopes.  $\times$  about 180.
4. Isolated egg from digested egg-ball, showing elongated inner shell containing six-hooked onchosphere.  $\times$  about 600.

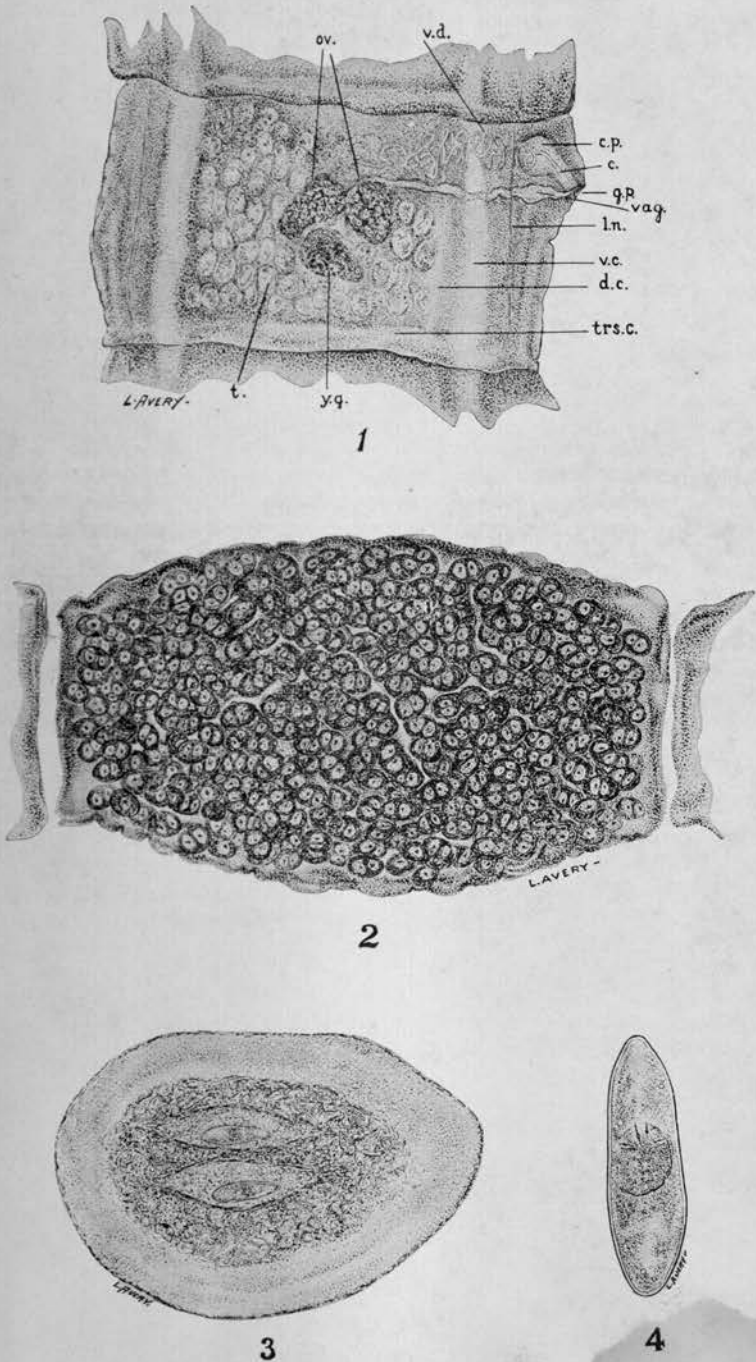


PLATE I.

A STUDY OF THE INFLUENCE OF RICE DIET AND OF IN-  
ANITION ON THE PRODUCTION OF MULTIPLE  
NEURITIS OF FOWLS AND THE BEARING  
THEREOF ON THE ETIOLOGY  
OF BERIBERI.<sup>1</sup>

By WESTON P. CHAMBERLAIN, HORACE D. BLOOMBERGH, and  
EDWIN D. KILBOURNE.<sup>2</sup>

- I. INTRODUCTION: RELATIONSHIP OF RICE TO BERIBERI AND POLY-  
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# I. INTRODUCTION: RELATIONSHIP OF RICE TO BERIBERI AND TO POLYNEURITIS GALLINARUM.

In 1896 Eykman<sup>(1)</sup> conducted feeding experiments with fowls and found that they would develop polyneuritis when fed on polished rice<sup>3</sup> but would not do so when given either *padi* (unhusked rice) or red rice. These experiments were repeated and verified later by Grijns,<sup>(2)</sup> Sakaki,<sup>(3)</sup> and others, and it was shown that the presence of a part of the pericarp or the addition of rice polishings would likewise prevent the disease in fowls.

Polyneuritis of fowls was then thought, and still is believed by many, to be analogous to beriberi of man, and since the fowl is easily experimented with, and is one of the very few animals thus affected, it became the favorite subject for feeding experiments in connection with beriberi.

However, there has always in the minds of many been a doubt whether these two diseases are truly analogous, and some have felt that experiments on man, or on an animal more closely related to man than the fowl, were necessary in order to learn much more about the etiology of beriberi.

Vordeman,<sup>(4)</sup> in 1895-96, in the prisons of Java fed polished and undermilled rice to different groups of men and succeeded in greatly reducing the number of cases of beriberi by the use of the latter variety, and he urged the substitution of red (undermilled) for white (polished) rice in the public institutions of Java.

Braddon<sup>(5)</sup> gave many additional instances of the ill effects of polished rice

<sup>3</sup>The endosperm of rice consists of starch except for a very thin outer portion called the aleurone layer which contains the albuminous material of the seed together with most of the fat. Outside of the aleurone layer is the pericarp or "inner skin" which varies in color from white to nearly black and in the Philippine rice is usually brick-red or yellowish-white. It contains most of the salts in the rice. Outside the pericarp is the husk. Unhusked rice is called by the English *padi* and in the Philippines *palay*.

If a rice have red pericarp and this is completely removed by milling, the resulting highly milled grain is as white as if a kernel with white pericarp had been treated in the same way. "Polished rice," "highly milled rice," "scoured rice," and "white rice" have been used by various writers as synonyms for rice deprived of its pericarp and most of its aleurone layer. The use of the term "white rice" in this sense is objectionable as liable to lead to confusion between milling processes and color of pericarp. The powder produced by grinding off the pericarp and the aleurone layer is called "polishings" in India, and in the Philippines *tiqui-tiqui*. "Undermilled rice," "medium milled rice," "unpolished rice," "Filipino No. 2 rice," and "red rice" are terms which have been applied to rices with considerable pericarp and aleurone layer left adherent to the grain.

As far as the presence of adherent pericarp is concerned undermilled rice corresponds with the "cured rice" of India. Cured rice has been parboiled and then dried before milling, the result being that the pericarp and aleurone layers are less easily removed in the mills. "Cured rice" is not used in the Philippines.

and the beriberi-preventing qualities of the parboiled or "cured" rice, but thought the former carried a toxin generated in it after milling.

Others, having in mind the evidence furnished by previous experiments and epidemics, felt that a privation theory would best account for the occurrence and distribution of beriberi, and experiments were conducted with prisoners, laborers, etc., to prove or disprove the correctness of their deductions.

It remained for Fraser and Stanton<sup>(6)</sup> in 1908-9 to prove beyond all reasonable doubt, in a series of experiments on laborers in the Malay Peninsula, that beriberi could absolutely be prevented by feeding "cured" (parboiled) rice, and that it would occur in the same places and under the same conditions when the men were given polished rice. Since these experiments it has been shown in many countries that the feeding of undermilled rice (which had not been parboiled) has the same beriberi-preventing influence as the use of the parboiled grain and that the beneficial effects of cured rice are due to the adherent pericarp and aleurone layer and not directly to the process of "curing."

As Fraser and Stanton so well put it,<sup>(7)</sup> "The fact that certain white rices when forming the staple of a diet in man produce beriberi rests on quite other testimony than that supplied by experiments on domestic fowls." As a result of their experiments on fowls they concluded<sup>(7)</sup> that while the etiologic connection of polished rice and beriberi was proved by previous experiments on man, the development of multiple neuritis in fowls when fed certain rices is an accurate indicator of the beriberi-producing powers of those rices.

Aron,<sup>(8)</sup> while not going so far, says, "These experiments give us a basis of investigation in order to ascertain the importance of the lack of certain food constituents (such as phosphorus) in producing pathologic changes in the nerves and other tissues."

## II. CHEMICAL COMPOSITION OF PHILIPPINE RICES.

Besides these biologic tests, it is now thought by many<sup>(7), (8), (9)</sup> that the phosphorus content is a good guide in the selection of a beriberi-preventing rice, but, as yet, no absolute standard has been adopted generally.

The officials of the Health Department in Hongkong consider that a rice will not cause beriberi if 0.4 per cent of phosphorus pentoxide is present. As a result of analyses, conducted in the Chemical Laboratory of the Bureau of Science in Manila, Aron considers that a rice is safe when it contains 0.45 per cent of phosphorus pentoxide and unsafe if it contains less than 0.35 per cent. An undermilled rice from Siam, called "Asylum No. IV," and which Dr. Hight has found by practical experience to be capable of preventing beriberi, was shown at the Bureau of Science to contain 0.52 per cent of phosphorus pentoxide.

Whether or not we consider lack of phosphorus to be the cause of beriberi it seems quite generally to be accepted that the amount of phosphorus in a given sample of rice is a reliable *index* of the beriberi-producing power of the grain when used as the principal article of the diet. Samples of the rices used in the succeeding experiments and also

samples of *tiqui-tiqui* were sent to the office of the Surgeon General of the Army for analysis as to the nitrogen, potassium, and phosphorus contents. Doctor Hodge's reports on them are shown in the following table:

TABLE I.—*Analyses of rices used in experiments.*<sup>a</sup>

Number.	Sample.	Per cent nitrogen.	Per cent potash= K <sub>2</sub> O.	Per cent phosphoric acid= P <sub>2</sub> O <sub>5</sub> .
1	Choice Saigon rice of Subsistence Department, polished	1.08	0.098	0.260
2	Filipino No. 1 rice, polished	1.19	0.093	0.255
3	Filipino No. 2 rice, yellowish-white pericarp, undermilled	1.20	0.271	0.576
4	Filipino No. 2 rice, red pericarp (Subsistence Department for Scouts), undermilled	1.32	0.223	0.489
5	<i>Tiqui-tiqui</i> , white	2.18	1.400	5.610
6	<i>Tiqui-tiqui</i> , red	1.87	0.973	2.588

It will be seen that numbers 1 and 2 (polished) did not differ very materially from numbers 3 and 4 (undermilled) as regards the nitrogen content but that there was a *great difference in the phosphorus and potassium contents of the polished and unpolished samples*, the latter having twice as much phosphorus pentoxide and two and a half times as much potassium oxide. It is of interest to note that the percentage of salts was lower in the red undermilled rice and the red *tiqui-tiqui* than it was in the white. This indicates a smaller proportion of salts for the red than for the white rice, but whether other analyses indicate such a difference we do not know.

Aron(8) gives the percentage of phosphorus pentoxide for various Philippine rices as follows: Laguna rice, unpolished, 0.557; same, polished, 0.314; "Macan" machinery rice, 0.340; same, native made, 0.455; "Valenciana" highly polished, 0.197; average Manila rice, 0.33. As regards polished and unpolished grades these analyses agree as closely as can be expected with those shown in the above table.

The analyses of our polished rices agree almost exactly with the "white rice" of Fraser and Stanton(7), (17) which contained 0.277 per cent of P<sub>2</sub>O<sub>5</sub>. Our undermilled rice contained more P<sub>2</sub>O<sub>5</sub> than the "parboiled rice" used by Fraser and Stanton, 0.489 and 0.576 per cent for ours as compared with 0.469 for theirs.

To select a rice which has beriberi-preventing qualities, it is not necessary to have a chemical analysis made. Whether the grain be a red or a white variety, a little experience will enable one to determine if sufficient pericarp is left on the kernel. In the case of rices with white pericarp, staining with Gram's iodine solution makes a selection more easy, since the pericarp does not take the stain, remaining grayish white, while the polished grains and the parts of the kernels denuded of pericarp become a deep blue, almost black.

<sup>a</sup>The nitrogen was determined by the Kjeldahl method, the potassium by the Lindo-Gladding.

## III. EXPERIMENTS ON FIFTY-SIX FOWLS.

Our experiments were begun to determine the effects of various Philippine rices on fowls and to use the knowledge thus acquired in the selection of a proper rice for issue to the native troops (Philippine Scouts). As they progressed, several additional experiments were instituted to throw light on some doubtful points observed in the original series, such as the relation of loss of weight and of inanition to multiple neuritis.

The fowls were kept separately in cages 5 feet by 5 feet, made of wire netting and wood; the floor, ceiling, and two sides being of pine boards, tongued and grooved, and the two remaining sides of wire netting with 2-inch meshes. A perch was placed across a corner of each cage about 20 inches from the floor. The cages were arranged in two separate structures each having eight cages, four below and four above. The roof was double with a large ventilating space between the two layers to render the conditions in the upper tier equal to those below. Figure 1 shows them very well. A high board fence around the yard prevented passers by from feeding the fowls. Clean water in enameled cups and a small amount of sterile gravel were kept in each cage. A run, 24 by 38 feet, inclosed by wire netting, adjoined the cages and in it were kept such extra fowls as were not in actual use.

During the course of the experiments six fowls developed infectious conjunctivitis which caused the death of five. From the clinical appearances we concluded that they were suffering from the so-called avian diphtheria which we do not consider to bear any relationship to human diphtheria.<sup>(21)</sup> Two other fowls also had the disease, accompanied by marked nose and throat symptoms. When any signs of this disease appeared, the infected fowls were promptly isolated and not used again for experiment, even if recovery took place. In Tables III and IV those having avian diphtheria are specifically referred to. Great care was taken to eliminate the possibility of this disease being the cause of death or of neuritis in the fowls undergoing experiment.

The sciatic nerves of all fowls dying during the experiments were placed, as soon as possible after death, in a 1 per cent osmic acid solution and subsequently were examined microscopically after being teased out in glycerine. The teasing was done with great care to avoid damaging structures which were really normal and thereby giving an appearance of slight degeneration. For controls the nerves of seventeen healthy chickens were examined by the same method. None of them presented the appearances of degeneration which were found in the fowls that clinically showed symptoms of neuritis.

Our birds were not especially selected as to breed, being the mixed varieties commonly seen in the Philippines, but were carefully inspected for soundness. Only cocks about three-fourths grown were accepted.

The experiments, covering a period of nine months, are given below. They are divided into four groups and fifteen classes, graphically arranged in Tables III and IV.

## GROUP A. TWENTY-NINE FOWLS SUBSISTING ON POLISHED RICE.

In this group of experiments two kinds of polished rice were used; a Philippine Macan rice, purchased in a native shop, and the Saigon variety furnished by the Subsistence Department of the Army, the

latter variety being that supplied the Philippine Scouts (native troops) from the date of their organization in 1901 until about September 1, 1910.

The Saigon rice was very thoroughly milled and polished, scarcely a trace of pericarp remaining on the grains, and in selecting the native polished rice (Filipino number 1) care was taken to obtain a quality similarly free from pericarp. Samples were rejected that showed yellow flakes of pericarp on the dark blue starchy interior, after staining the grains in Gram's iodine solution. The particles of pericarp remaining on the grains of incompletely milled red rice were plainly seen without staining, making easy the detection of unsuitable varieties.

These two kinds of rice, Saigon and Filipino polished, were fed alone in some of the experiments and in others were mixed together and fed in various combinations with salts of potassium and of phosphorus. Phosphorus and potassium were used because by some previous work<sup>(10)</sup> we had shown that these elements were deficient in the diets of the companies of Filipino Scouts having beriberi, and that the deficiency was directly proportionate to the incidence of the disease in those companies.

*Class 1. Fed on Filipino number 1 rice.*—Five fowls were put on a diet consisting of polished native Macan rice (Filipino number 1). By analysis it contained 0.093 per cent of potassium oxide and 0.255 per cent of phosphorus pentoxide. One of these fowls died on the 22d day of avian diphtheria, without signs of neuritis (number 1) and the other four (numbers 2, 3, 4, and 20) developed multiple neuritis after 25 to 33 days (average 29 days) and died on the 30th to 41st day (average 36th day).

None of the fowls seemed to care for this rice after the 3d or 4th day and seldom ate their daily allowance of 118 grams. They declined rapidly in weight, losing an average of 26.3 per cent up to the time of the appearance of the signs of neuritis in the legs and an average of 37.6 per cent to death. Their weight curves are shown on Chart 1.

The signs of multiple neuritis were well marked in these four fowls and, in corroboration, on *post-mortem* microscopic examination their sciatic nerves showed extensive degeneration. Microscopic examination of the nerve of a fowl (number 1) dying of acute respiratory trouble, now thought by us to be avian diphtheria because of our subsequent findings in similar cases, showed no degeneration.

*Class 2. Fed on Saigon polished rice of the Subsistence Department.*—This rice showed on analysis 0.098 per cent of potassium oxide and 0.260 per cent of phosphorus pentoxide. Four fowls were fed on it. Three (numbers 5, 6, and 8) developed multiple neuritis after 25 to 39 days (average 31 days) and two died on the 31st and 36th day respectively (average 33 days). One (number 7) was found dead in his cage after a severe wind and rain storm. He seemed perfectly well the day before and at no time had shown any signs of neuritis.

This class contains two very interesting birds, numbers 5 and 7, and as they are worthy of more than passing notice their histories are given in detail.

Number 5<sup>\*</sup> was purchased May 10, 1910, kept under observation for five days

<sup>\*</sup> Shown September 5, 1910, to the Manila Medical Society.

in a cage and fed on *palay* (unhusked rice) and kitchen stuff composed of scraps of meat, bread, and vegetables. He was then fed on Saigon polished rice, being allowed 118 grams of rice daily, and, unlike most of the fowls we have used, he ate it all day after day.

He did well until June 23, the 39th day, when he staggered slightly on turning. July 2, the 48th day, he was observed to go down on his knees\* after exertion. From the 48th to the 90th days he remained about the same, showing his trouble after exercise, but doing very well when not hurried. On August 12, the 90th day, he showed pronounced and typical signs of neuritis, namely, drooping of the wings and inability to keep the legs extended at the knee.

His weight, shown on Chart 1, ran as follows:

Date.	Day.	Grams.	Remarks.
May 16	1st		Saigon rice begun.
May 21	6th	878	
June 1	17th	786	
June 11	27th	722	
June 18	34th	736	
June 23	39th	630	Staggers.
July 2	48th	701	Occasionally on knees.
July 9	55th	687	
July 16	62d	694	
July 23	69th	708	
July 30	76th	708	
August 6	83d	637	Mixed feeding begun.
August 12	89th	623	
August 20	97th	666	
August 27	104th	715	
September 4	112th	722	
September 6	114th	710	Chloroformed

On the 39th day, when the earliest signs of neuritis appeared, he had lost 22.6 per cent of body weight. From this day to the 76th he remained almost stationary, but from that time on began to lose rapidly until on the 90th day, when the signs of multiple neuritis were marked, he had lost 29.1 per cent.

On the 90th day this fowl (number 5) was given a mixed diet of *palay* and kitchen stuff, in an effort to save him so as to see whether or not spasticity would supervene, as it had in the case of another fowl (number 17) similarly saved from death by mixed diet after the development of neuritis. It had been our experience that fowls went on rapidly to death after acquiring multiple neuritis, rarely living more than five or six days, but in this case (number 5) we were able to save the fowl, and, while his general condition greatly improved from the first, the signs of neuritis grew more marked for several days and then remained stationary until the 114th day, when he was chloroformed.

In addition to the usual leg and wing signs of neuritis there gradually developed a spastic gait. The fowl would stand and walk with knees stiff, teetering forward on the toes, and with the ball of the foot scarcely touching the ground. In an effort to maintain his balance he would take short, quick steps, and seemed to carry the body so far forward that his feet had to hurry to keep up. Figures 2 and 3 are from photographs taken to show the spasticity, but unfortunately do not give a very good idea of it.

\* In this paper "knees" means the joint formed by the tibio-tarsus and tarso-metatarsus.

We have not been able to find any mention of this spasticity in the literature on the subject. It did not appear in any of our fowls fed on the same rice as number 5 and allowed to go on to death. Evidently it occurs late in the disease. Holst<sup>(11)</sup> speaks of finding some slight degeneration in the white matter of the spinal cord in fowls dead of polyneuritis but does not mention a spasticity of gait observed before death. Microscopic examination of sections of the cord from fowl number 5 showed no degeneration in any of the tracts. The sciatic nerves were extensively degenerated.

Fowl number 7 of this class was remarkable in that he remained well for 89 days on polished rice, showing no sign of neuritis before death, which resulted from exposure in a storm.

In all our experiments with polished rice we have found that those fowls which ate well would remain free from neuritis for much longer periods than the average in whom anorexia with refusal of food appeared early. More will be said on this phase of the subject later in connection with our starvation work in classes 13, 14, and 15. Fowl number 7 ate well from the beginning and always consumed his daily allowance of 118 grams.

His weight, shown on Chart 1, ran as follows:

Date.	Day.	Grams.	Remarks.
May 16 .....	1st .....	.....	Saigon rice begun.
May 21 .....	5th .....	1,162	
June 1 .....	11th .....	1,162	
June 11 .....	21st .....	1,091	
June 18 .....	28th .....	1,071	
June 25 .....	35th .....	1,162	
July 2 .....	42d .....	1,119	
July 9 .....	49th .....	1,119	
July 16 .....	56th .....	1,140	
July 23 .....	63d .....	1,091	
July 30 .....	70th .....	1,098	
August 6 .....	77th .....	1,048	
August 12 .....	83d .....	1,020	
			Found dead.

Microscopic examination of the sciatic nerves showed slight degenerative changes.

The characteristic attitude in polyneuritis, gallinarum is shown in figures 4, 5, 6, 7, and 8, which are reproduced from photographs of fowls numbers 6 and 8 of this class.

*Class 3. Fed on 118 grams of polished rice, given by force when necessary.*—In view of the fact that most of the fowls soon tired of polished-rice, ate only a small part of their daily allowance, and went rapidly to neuritis and death, we decided to study a series of four which were given polished rice, feeding the fowls 118 grams daily, by force when it was not eaten voluntarily. This amount, 118 grams, was selected because the birds that ate well and remained nearly stationary in weight consumed about that quantity.

The polished rice used was the Saigon grain supplied by the Subsistence Department, and was fed raw and dry. When necessary to use force it was pushed into the crop with the end of the little finger.

It is doubtful if this maneuver was of any use. The bird's appetite was probably a good indication of their ability to digest and assimilate polished rice, and an excess was probably not used.

Of the four fowls thus fed, three (numbers 45, 48, and 49) ate but little voluntarily, speedily lost in weight, and developed multiple neuritis in 27 to 31 days (average 29.6 days) and two of them died on the 42d and 63d day respectively. After showing well-marked signs of neuritis they were given *palay* and kitchen stuff without avail in two cases, which soon thereafter died. One (number 48) was saved by the mixed feeding and, one and one-half months later, had practically recovered the use of his legs and wings. He showed no spasticity at any time. When he had nearly recovered from the neuritis he was turned loose.

The fourth (number 40) differed from the others in that *he ate his full daily allowance and weighed more at the end than at the commencement of the experiment. He did not show any signs of nerve involvement.* He was released on the 81st day of the experiment.

The weight curves of the fowls forcibly fed are shown on Chart 2. It will be seen that the fowl remaining well (number 40) gradually regained the 11.1 per cent of his original weight, which he had lost during the first month.

#### POLISHED RICE COMBINED WITH VARIOUS SALTS.

In an attempt to explain the etiologic connection between polished rice and beriberi, the kinds and quantities of inorganic and organic salts present have received a large share of attention. Schauman and others<sup>(8)</sup>, <sup>(9)</sup> believe that beriberi results from phosphorus privation. Some<sup>(12)</sup> have suggested poisoning by, or a lack of, other salts, inorganic and organic, and others have thought that too little of certain proteids or enzymes may be etiologic factors.

After investigating the dietaries of the native troop (Philippine Scouts), the United States Army Board for the Study of Tropical Diseases as they Exist in the Philippines found that the amounts of phosphorus and potassium consumed were deficient in the companies having beriberi, and varied inversely with the incidence of the disease. In our former report on this subject<sup>(10)</sup> the companies were divided into three classes, as follows:

TABLE II.—Average number of grams consumed per man per day.

Class.	P <sub>2</sub> O <sub>5</sub> .	KCl.
1. Having many cases.....	3.3474	1.0600
2. Having a few scattered cases.....	3.9399	1.1905
3. Having no cases.....	4.6279	1.6517

The amounts of P<sub>2</sub>O<sub>5</sub> average 3.3474 grams in the bad companies, 3.9399 in those slightly affected, and 4.6279 in the companies for the prisoners having no beriberi; a difference of 1.2805 grams between the worst and best averages.

The amounts of potassium chloride average 1.06 grams in the worst, 1.1905 in the medium, and 1.6517 grams in the best organization, a difference of 0.5917 gram between the worst and the best.

These amounts of potassium chloride do not run exactly parallel to the phosphorus content of the three groups, there being a greater relative difference in the amounts of the former. The increase of the best over the worst was 56.76 per cent in the potassium chloride, but only 38.22 per cent in phosphorus pentoxide.

In a set of experiments with fowls we added salts of potassium and phosphoric acid to the diets of polished rice, as follows:

Class 4. Polished rice + 0.05 gram KCl daily.

Class 5. Polished rice + 0.03 gram  $\text{H}_3\text{PO}_4$  daily.

Class 6. Polished rice + 0.06 gram  $\text{H}_3\text{PO}_4$  daily.

Class 7. Polished rice + 0.05 gram KCl and 0.03 grams  $\text{H}_3\text{PO}_4$  daily.

Class 8. Polished rice + 0.03 gram  $\text{H}_3\text{PO}_4$  substituted later by 0.05 grams KCl daily.

In determining the amounts of the salts to be fed, the quantities found to be consumed by the Scouts from the organizations having no beriberi were reduced to correspond to the average weight of the fowls and a small amount added to provide a safe margin. Of course, we have nothing to show the requirements of fowls and they may differ considerably from the human.

The different salts were administered in solutions of such strength that one cubic centimeter of each contained the required dose.

In these experiments with polished rice combined with various salts, we made no attempt to use organic phosphorus in the form of phytic acid or phytin (calcium-magnesium salt of phytic acid) because, first, it was not convenient to obtain these substances and, second, the experiments recently conducted by Aron(8) and Kajiura and Rosenheim(20) indicated to our minds that no beneficial results were likely to be obtained from their use. This opinion has just been confirmed by the experiments of Fraser and Stanton,(22) who found that phytin would not prevent neuritis.

*Class 4. Fed on polished rice + 0.05 gram potassium chloride daily.*—Four fowls were used and all developed multiple neuritis in 22 to 33 days (average 30.5 days) and died on the 29th to 44th day (average 37.5 days).

The weight curves of these fowls (numbers 21, 22, 23, and 24) are shown on Chart 3. The average loss of body weight to the time of the appearance of neuritis was 28.0 per cent and to death 43.8 per cent.

It will be obvious, on glancing at the steep descent of these curves and on considering the time intervening between the commencement of the experiment and the occurrence of neuritis and death, that the administration of potassium chloride was of no avail, the "incubation period" and length of life being practically the same as for fowls fed on polished rice alone.

*Class 5. Fed on polished rice + 0.03 gram phosphoric acid daily.*—Three fowls were put on this diet, and all died after developing typical neuritis. The leg signs appeared after 22 to 27 days (average 23 days) and death occurred on the 27th to 34th (average 30.3 days).

Their weight curves are shown on Chart 3 as numbers 25, 26, and 28. An average loss of 28.2 per cent occurred to the appearance of signs of neuritis and 40.3 per cent of death.

Nothing worthy of special mention was noted among these fowls except that *they developed multiple neuritis and died in a shorter period than those on polished rice alone.*

*Class 6. Fed on polished rice + 0.06 gram phosphoric acid daily.*—After observing the shortness of the "incubation period" and the rapidity with which death supervened in the fowls of the preceding class, fed on polished rice combined with 0.03 gram phosphoric acid and to throw some light, if possible, on the reason for this, a set of three fowls was fed the same kind of rice with a daily addition of double the amount of phosphoric acid or 0.06 gram.

Of these three fowls two developed typical leg signs, one (number 60) on the 27th day and one (number 59) on the 31st day (average 29th day).

Instead of allowing them to go on to death we fed them *palay* and kitchen stuff on the 30th and 34th days respectively and, as in the case of fowl number 5, greatly improved their general condition without in any way lessening the signs of multiple neuritis. Both of them also developed spasticity like that observed in number 5 and described in connection with that fowl.

These two fowls were eventually chloroformed. The sciatic nerves showed marked degenerative changes. No evidences of degeneration were found in the tracts of the spinal cords.

Their weight curves, Chart 4, resemble those of fowls fed on polished rice alone. An average loss of 25.2 per cent occurred to the appearance of signs of neuritis and of 30.2 per cent to the end of the experiment, that is to the beginning of mixed feeding.

The fowls of this class kept well nearly a week longer than those on the same rice with one-half the amount of phosphoric acid, but probably this was a mere coincidence, for they fared no better than those of classes 1 and 2 fed only polished rice. The third fowls of this class (number 61) died of avian diphtheria, the lesions being in the nose. Nothing abnormal was found in the sciatic nerves.

*Class 7. Fed on polished rice + 0.03 gram phosphoric acid and 0.05 gram potassium chloride daily.*—In this class the same rice was used as in classes 5 and 6 and the solutions of the two salts were given at different times during the day.

Of the five fowls, three (numbers 29, 31, and 32) developed multiple neuritis in from 21 to 28 days (average 25.3 days) and died on the 25th to 34th day (average 30th day).

The reduction in weight to the appearance of signs of neuritis averaged 32.4 per cent and to death 40.9 per cent.

Two of the birds (numbers 30 and 37) contracted infectious conjunctivitis and died, without signs of neuritis, one on the 4th day and the other on the 24th day of the experiment.

*Class 8. Fed on polished rice + 0.03 gram phosphoric acid for 34 days and 0.05 gram potassium chloride for 91 days.*—One fowl (number 27) was fed in a manner like those of class 5 for 34 days and then, through accident, the acid was replaced by 0.05 gram potassium chloride. It was kept on polished rice and these salts for 125 days, and then weighed but little less than at the commencement of the experiment, and was apparently as vigorous and well as when first placed in his cage.

We do not ascribe his continued good health to the salts but to the fact that he liked polished rice and greedily devoured all that was given him. Only a

few of our fowls have voluntarily eaten freely of this rice and these have been able, by so doing, to maintain their body weight and defer or altogether prevent the development of multiple neuritis.

Number 27 weighed 1,098 grams at the beginning of the experiment and after 125 days weighed 998 grams. A loss of about 15 per cent occurred in the 34 days during which he received phosphoric acid with his rice, and a steady gain took place after the substitution of the solution of potassium chloride; whether or not merely coincidental we are unable to say.

The average time to neuritis of the fowls of all the groups receiving phosphoric acid was 25.3 days as compared with 29.8 days, the corresponding time for those on polished rice alone, and similarly the fowls on phosphoric acid died in an average time of 30.2 days as against 34.7 days when fed polished rice alone.

Food.	Average time to neuritis.	Average time to death.
	<i>Days.</i>	<i>Days.</i>
Polished rice alone.....	29.8	34.7
Polished rice + phosphoric acid.....	25.3	30.2

The difference in favor of polished rice alone is small and may have been due to idiosyncracies of the fowls, or to other factors. *The table shows that the administration of this form of inorganic phosphorus is of no avail in preventing neuritis*, for, if such were the case, the fowls receiving it should have remained well much longer than those fed on polished rice alone, whereas they became sick on an average of 4½ days sooner.

#### GROUP B. THIRTEEN FOWLS SUBSISTING ON UNDERMILLED RICE.

Two kinds of undermilled rice were used, a Filipino "Macan" rice having a yellowish-white pericarp, and a native mixed rice with about one red grain to every four of the yellow grains. Both kinds were only partially milled, more than half the surface of the grains being covered with pericarp. The second or mixed variety is that now supplied, on the recommendation of this Board, to the Philippine Scouts.

Three classes of experiments were made, first (class 9), those on the first variety of undermilled rice; second (class 10), those on the second; and third (class 11), those on the first plus 0.36 gram sodium chloride daily.

*Class 9. Fed on undermilled rice having a yellowish-white pericarp.*—The rice had 0.271 per cent of potassium oxide and 0.576 per cent of phosphorus pentoxide. Four fowls remained well on this diet for 79 days. None showed the slightest signs of neuritis or other sickness and were in good condition when taken out of the cages. (Numbers 9, 10, 11, and 12.)

Three of the four gained in weight from 4.2 to 17.9 per cent (average 9.4 per cent) while the remaining one lost 17.2 per cent.

*Class 10. Fed on undermilled rice having a red pericarp.*—The rice used in this experiment was that supplied by the Subsistence Department of the Army to the native troops (Philippine Scouts). It contained 0.223 per cent of potassium oxide and 0.489 per cent of phosphorus pentoxide.

Three out of four fowls have remained in perfect health on this diet for an average time of 129.6 days. (Numbers 38, 39, and 47.) The fourth (number 46) acquired infectious conjunctivitis and died, without signs of neuritis, on the 26th day.

The three healthy birds gained in weight from 22.8 per cent to 37.3 per cent (average 29.2 per cent) while subsisting solely on this unpolished rice.

*Class 11. Fed on undermilled rice (yellowish-white) + 0.36 gram sodium chloride daily.*—Bunge in 1894(13) called attention to the relationship of the potassium and sodium salts of the food to each other, maintaining that an excess of potassium carbonate when ingested will react with sodium chloride forming sodium carbonate and potassium chloride which are soluble and are eliminated in the urine, thereby depriving the system of needed elements.

Loeb(14) has shown the necessity for a balance between the sodium, calcium and potassium ions, and that the calcium and potassium ions counteract the effects of the sodium ions in the blood. When marine animals were placed in a pure solution of sodium chloride of the same concentration as sea water, their muscular contractility was lost. Small amounts of calcium and potassium ions antagonized the poisonous effects of the sodium ions.

Le Dantec(15) in the course of experimental work with fowls noticed that the multiple neuritis produced when they were fed on polished rice was seldom (2 cases in 60) accompanied by the oedema which is so frequently observed in the beriberi of man. Desiring to produce this oedema he injected a solution of sodium chloride into the pectoral muscles and killed the birds in every case. He found that it also had the same effect when injected into starving fowls. He made no mention of having administered the salt to fowls not in a cachectic state.

As stated before when describing our experiments with polished rice and various salts, we previously found(10) that the dietaries of the Scout companies having beriberi were deficient in potassium and phosphorus. We also found that the Scouts were rather heavy salt eaters and suggested that this habit may have had an etiologic connection with beriberi by abstracting needed potassium ions.

In class 11 we fed five of our fowls a rice proved by previous experiments (class 9) to prevent neuritis, and in addition gave a daily dose of 0.36 gram of sodium chloride in solution, the amount being decided upon in a similar manner to the determination of the amounts of potassium and phosphorus used in classes 4, 5, 6, 7, and 8. On the 55th day the amount of sodium chloride was increased to 0.72 gram daily.

Four of the five birds continued well, remained stationary or slightly gained in weight, and after an average time of 113.2 days, showed no signs of neuritis. (Numbers 33, 35, 36, and 58.) One fowl (number 34), after nearly two months of apparent health, acquired infectious conjunctivitis and died on the 61st day with a loss of 26.5 per cent of body weight.

*The administration of sodium chloride in either dose, 0.36 or 0.72 gram, seemed to have no effect on these fowls, but it must be remembered that they were strong animals, receiving a neuritis-preventing rice, were in fine condition, and not cachectic like those of Le Dantec.*

## GROUP C. FOUR FOWLS SUBSISTING ON UNHUSKED RICE.

*Class 12. Fed on palay or padi.*—Although unhusked rice has been proved by numerous experiments outside of the Philippines to prevent polyneuritis galinarum, we undertook these tests with the native Macan unhusked rice to see whether or not it possessed the same qualities as the *padi* of other countries and to control the experiments of classes 1, 2, and 9 which were going on simultaneously.

Eighty-one grams of unhusked rice, called *palay* in the native Tagalog dialect, were fed daily to each of four fowls and all remained well to the end of the experiment, 79 days, and showed no abnormal signs. (Numbers 13, 14, 15, and 16.)

A loss of 17.9 per cent and 18.9 per cent of body weight occurred in two of the birds and a gain of 0.6 per cent and 5.6 per cent in the others.

## GROUP D. TEN FOWLS UNDERGOING STARVATION.

As our experiments progressed we noticed that the development of neuritis was invariably accompanied by a considerable loss of weight. In no case did a fowl acquire the disease while gaining or while remaining stationary in weight, indeed, a reduction of 21 per cent or more, except in the cases of fowls numbers 2 and 20, seemed a necessary accompaniment of neuritis. In consequence we decided to feed some fowls reduced amounts of a neuritis-preventing rice and to give others water alone, with the purpose of producing, if possible, a neuritis as a result of partial or complete starvation. That this was accomplished is shown by the following experiments.

*Class 13. Fed on undermilled rice with yellowish-white pericarp. Fifty-two grams (one-half usual allowance) daily for 43 days; followed by 26 grams for 47 days and 13 grams for 25 days.*—One fowl (number 18) was fed 52 grams daily of the neuritis-preventing rice used in class 9, this amount being one-half the daily allowance given the fowls in that class, all of which remained healthy.

With this amount he was able to almost maintain his original weight, losing only a small amount in 43 days. The quantity of rice given was then reduced to 26 grams and from that time a considerable loss of weight occurred, but to hasten the result this was further reduced to 13 grams on the 90th day.

The fowl continued in good condition, except for general weakness which began to be evident about the 90th day, until the 107th day when weakness was particularly manifest in the legs. On the 115th day he was unable to rise, whether from neuritis or general weakness we were unable to say. To determine if possible the condition of his nerves he was then given *palay* and kitchen stuff and rapidly improved except in the legs. He became strong enough to stand, ate well and seemed bright and interested in his surroundings, but had the typical gait and leg signs of neuritis, which became more marked during the two or three days following resumption of mixed diet. He died suddenly on the 122d day. His characteristic attitude is well shown in the pictures, figures 9 and 10.

On microscopic examination his sciatic nerves showed slight degenerative changes.

When signs of neuritis were unmistakable he had lost 46.6 per cent of body weight; at death he had lost 49.4 per cent. His weight curve is shown on Chart 5 as number 18.

*Class 14. Fed on undermilled rice with yellowish-white pericarp, 26 grams (one-fourth usual allowance).—*Fowl number 19<sup>1</sup> was given a ration of 26 grams of the same undermilled rice as was used in classes 9, 11, and 13, and this amount, one-fourth that fed in class 9, was continued unchanged throughout the experiment.

A steady and progressive reduction of weight followed accompanied by increasing weakness. His weight curve shown on Chart 5 as number 19, ran as follows:

Date.	Day.	Grams.	Remarks.
July 14 -----	1st -----	842	One-fourth allowance begun.
July 16 -----	3d -----	821	
July 22 -----	9th -----	765	
July 23 -----	10th -----	751	
July 26 -----	13th -----	736	
July 30 -----	17th -----	694	
August 3 -----	21st -----	659	
August 6 -----	24th -----	595	Died.
August 14 -----	32d -----	538	

On August 11, the 29th day, he seemed disinclined to move, two days later showed well marked early signs of neuritis, and on the following day died. In this case no attempt to save by mixed feeding was made.

A loss of 34.7 per cent to the time of signs of neuritis and 39.5 per cent to death occurred.

The sciatic nerves were extensively degenerated.

*Class 15. Water only.*—In a previous publication<sup>(16)</sup> we reported a case of typical multiple neuritis in a fowl that had been given water, but no food, and stated that the same experiments would be continued with a larger number of birds. In all we experimented with 8 fowls and *unmistakably produced the disease in three*. Two others very probably had the disease, but we were unable to save them by mixed feeding so could not obtain a clear clinical picture because the signs of neuritis were obscured by those of general weakness. *However, the nerves of these two fowls showed degeneration.*

The histories of these 8 fowls follow and are given somewhat in detail.

Fowl number 17 was purchased May 10, 1910, and kept in a cage on mixed diet, consisting of *palay*, undermilled rice and kitchen stuff, until July 14, when all food was stopped. After July 14, he was allowed only water.

The first signs of trouble were noted on July 26, the 13th day of his fast. He had difficulty in jumping to his perch. On the 21st day he could not get up to it at all. When not disturbed he would stand with head close to the body and eyes closed, but was not observed sitting on his knees. On the 23d day he stood as above and with his knees very straight. When made to walk he showed a tendency to teeter forward. He was evidently very weak and we were unable to feel certain whether his condition was due to pure weakness or to something else. It was feared he would die within 24 hours if he were not

<sup>1</sup>This fowl was reported in a paper read before the Manila Medical Society September 5, 1910, and published in the September *Bull. Manila Med. Soc.* (1910).

fed, consequently we determined to resume feeding with a neuritis-preventing food in the hope that we could save him and make sure that the leg signs were not due solely to weakness. This we accomplished. August 6, the day following the resumption of food, the signs of neuritis were greatly increased and left no doubt as to the nature of his trouble. The characteristic attitude is well shown in the figures 11 and 12.

During the following days, in which *palay*, undermilled native rice, and kitchen stuff were fed, the leg and wing signs became worse, but his general condition improved rapidly. He became bright-eyed, interested in his surroundings, and gained in weight. His appetite needed no stimulation. The peculiar spasticity he had exhibited at the end of the starvation period increased until walking was performed on his toes, with knees almost straight. An effort to photograph and show the spastic gait was only partially successful. During the last week of his life this fowl partially regained the use of his right leg.

On the 55th day he was chloroformed and the sciatic nerves and spinal cord removed for microscopic examination. The sciatic nerves showed extensive degeneration. No areas of degeneration were found in cross sections of the cord.

His weight, shown on Chart 5, ran as follows:

Date.	Day.	Grams.	Remarks.
July 14 -----	1st -----	991	Starvation begun.
July 16 -----	3d -----	921	
July 22 -----	9th -----	786	
July 23 -----	10th -----	772	
July 26 -----	13th -----	722	
July 30 -----	17th -----	687	
August 3 -----	21st -----	595	Mixed feeding begun.
August 5 -----	23d -----	-----	
August 14 -----	32d -----	687	
August 20 -----	38th -----	715	
August 27 -----	45th -----	708	
September 4 -----	53d -----	744	
September 6 -----	55th -----	730	Chloroformed.

His loss of weight to the appearance of signs of neuritis was 27.2 per cent and at the end of the starvation period had increased to 40.0 per cent.

Fowl number 41 was put on water alone September 10, 1910. Nothing of importance was noted until September 13 when he became sick with avian diphtheria and died of this infection 5 days later, September 18.

His loss of weight amounted to 39.4 per cent.

Microscopic examination of his nerves showed slight degeneration. No clinical signs of multiple neuritis were observed before death.

Fowl number 42. The water diet was instituted September 10 and was followed by a steady and rapid reduction of weight and muscular strength. On September 26, the 16th day, he was very weak, could not stand, and, when prodded, would not move his legs or wings. Although the general weakness was great we were of the opinion that there was probably, in addition, a peripheral nerve involvement. It was thought that he was not too far gone to revive with mixed feeding and a diet consisting of *palay* and kitchen stuff was then instituted, but without favorable result, for he was found dead in the cage the next morning, the 18th day.

His weight ran as follows:

Date.	Day.	Grams.	Remarks.
September 10-----	1st-----	963	Starvation begun.
September 18-----	9th-----	835	
September 21-----	15th-----	602	
September 26-----	17th-----	524	Mixed feeding begun.
September 27-----	18th-----	524	Found dead.

A reduction of 45.6 per cent had occurred when the mixed diet was begun and it is probable that starvation in the case of this fowl was carried too far.

Microscopic examination showed some degeneration of the sciatic nerves.

Fowl number 43 died suddenly on the 14th day of the experiment without having shown any signs of neuritis. The day before his death he showed some general weakness and could not jump up onto his perch, but, on the whole, was in fair condition and we did not anticipate his early demise.

A reduction of 37.6 per cent in weight was observed in his case.

The sciatic nerves were not degenerated.

Fowl number 44. Starvation was begun September 10, water only being allowed. On September 26, the 17th day, he lay on the floor of the cage most of the time; when prodded he would stand and walk a short distance. The gait was that of early neuritis and we had no doubt of its existence. Our belief was corroborated by the *finding of extensive degeneration* upon microscopic examination of the nerves after death, which occurred September 27, the 19th day of the experiment and one day after mixed feeding was begun.

His weight ran as follows:

Date.	Day.	Grams.	Remarks.
September 10-----	1st-----	970	Starvation begun.
September 18-----	9th-----	807	
September 24-----	15th-----	616	
September 26-----	17th-----	582	Mixed feeding begun.
September 27-----	18th-----	531	Died.

A loss of 40.0 per cent to the appearance of signs of neuritis, and of 45.3 per cent to death was noted.

No doubt we were unable to save this fowl because inanition was allowed to progress too far.

Fowl number 54. Little need be said of this fowl, for his death occurred suddenly, through an accident, while apparently doing well.

On the 11th day of his fast he seemed in good condition except for some weakness, but the following morning he was found dead with his head and one leg through a small hole in the bottom of the cage. During this time a loss in body weight of 29.8 per cent had occurred.

No degeneration was seen in his sciatic nerves.

Fowl number 55 was kept in one of the cages and fed a mixed diet of *palay* and kitchen stuff for three weeks and then, October 21, given water but no food. Like the other starved fowls he lost rapidly in weight and became progressively weaker until November 5, the 16th day, when feeding with *palay* and kitchen stuff was resumed. On that day he was very weak and lay on his side on the floor

with his eyes closed the greater part of the time. When prodded with a stick he could be made to stand for a very short time. The comb and wattles were deeply cyanosed and his whole appearance was that of a fowl very near to death.

When the grains of *palay* were put before him he would greedily devour them. From that time he improved in general condition, but like number 17 showed more marked signs of neuritis during the succeeding days; unlike that fowl, he did not show spasticity. At this stage pictures were taken which show the usual positions assumed by fowls with the disease. (Figures 13 and 14.) After 9 days of this mixed diet his gait had improved somewhat, but not more so than that of several fowls similarly saved from death after they had developed marked signs of neuritis when fed on polished rice.

He was chloroformed on November 16, the 27th day, and the sciatic nerve removed for microscopic examination; it showed degeneration.

His weight, shown on Chart 5, ran as follows:

Date.	Day.	Grams.	Remarks.
October 21.....	1st.....	963	Starvation begun.
October 30.....	10th.....	892	
November 5.....	16th.....	700	Mixed feeding begun.
November 12.....	23d.....	729	
November 16.....	27th.....	800	Chloroformed.

On the 16th day, when signs of neuritis appeared and the mixed feeding was begun, he had lost 27.4 per cent of his body weight.

Fowl number 56. The clinical history of this bird much resembles that of number 42.

October 21 starvation, except for water, was begun and continued until November 1, the 12th day, when a mixed diet of *palay* and kitchen stuff was given. This fowl declined in weight very rapidly and although starved only 12 days had then lost 44.6 per cent. He died on November 2, the 13th day, after one day of mixed diet. The appearance of this bird was similar to that of number 42; while the signs of nerve involvement seemed present, the general weakness was so great that we could not be positive on this point. However, on microscopic examination the sciatic nerves proved to be moderately degenerated.

#### SUMMARY OF STARVATION EXPERIMENTS.

Two fowls (numbers 18 and 19) were fed reduced quantities of a neuritis-preventing, undermilled rice and both developed multiple neuritis. Eight fowls allowed nothing but water gave three positive cases (numbers 17, 44, and 55), two doubtful (numbers 42 and 56), and three negative ones (numbers 41, 43, and 54).

#### IV. GENERAL CONSIDERATION OF MULTIPLE NEURITIS IN STARVED FOWLS.

Eykman<sup>(1)</sup> did not find polyneuritis in chickens fed on such small quantities of undermilled rice that they died from starvation. Sakaki<sup>(3)</sup> also stated that the weakness in starvation progressed to death without any staggering or other signs of neuritis. Holst<sup>(11)</sup> in speaking of Eykman's nonobservance of polyneuritis in chickens starved on small amounts of undermilled rice, says, "Nor have I found any polyneuritis myself, experimenting in a similar way with pigeons." Likewise Fraser and Stanton<sup>(17)</sup> say in this connection, "Fowls

receiving nothing but water do not develop polyneuritis, while fowls receiving only polished rice and water do."

The only statement to the contrary, we have found in the literature, is that made in the discussion of the beriberi papers<sup>(18)</sup> by Dr. Gorosaku Shibayama, delegate from His Imperial Japanese Majesty's Government to the meeting of the Far Eastern Association of Tropical Medicine, held at Manila, March 5, 1910. He said, "Polyneuritis accompanies general cachexia and inanition in fowls, whereas beriberi, especially the acute, pernicious form, generally attacks well-nourished muscular men."

This statement agrees exactly with the findings in our starvation experiments, and we believe the reason the evidences of neuritis were overlooked by other workers is that *they appear very shortly before death and are obscured by the signs of general weakness*. It is not an easy matter to resume feeding at exactly the proper moment to save the animal and leave the neuritis well developed.

#### V. RELATION OF LOSS OF WEIGHT TO DEVELOPMENT OF POLYNEURITIS GALLINARUM.

The amount an animal can lose and still live varies somewhat with the individual. Withington,<sup>(19)</sup> in discussing starvation, refers to the following:

Chossat stated that the total proportional weight loss of an animal dying of inanition was 40 per cent of the initial weight. But further experiments have shown that a fat animal may lose 50 per cent of its weight, while a lean one can lose only 35 per cent. Young animals in a growing stage have been observed to lose only 30 per cent before they succumbed.

\* \* \* \* \*

The ingestion of water, then, while postponing the fatal result of a fast, produces no important change in the mode of death from that which occurs in simple inanition.

Le Dantec says that in polyneuritis of fowls, when fed on polished rice, the loss of weight is progressive and death occurs when the animals have lost about one-third of their body weight.

Our two fowls, numbers 18 and 19, fed on reduced amounts of un-dermilled rice, lost an average of 40.6 per cent to the end of the experiment, which was death in the case of number 19, and rescue by resuming full diet in the case of the other, number 18.

Those which developed easily recognized signs of multiple neuritis while being given only water, numbers 17, 44, and 55, lost on an average 31.5 per cent up to the time of the appearance of the disease and 37.5 per cent to the end of the starvation period when feeding was resumed. *The losses in this class correspond very closely with those of classes 1, 2, and 3 in which the fowls developed the disease on polished rice alone and where the decrease in weight averaged 31.6 per cent to the appearance of signs of neuritis and 39.9 per cent to the end of the experiment, which was death in the case of eight and salvation by mixed feeding in two out of the ten fowls.*

One can not avoid wondering if the real cause of multiple neuritis in fowls fed on polished rice is not general inanition rather than the lack of any one element in the rice. LeDantec<sup>(15)</sup> says "Fowls nourished on white rice die of inanition and not of beriberi." A similar view is expressed by Breaudat<sup>(23)</sup> who states that animals so nourished die of inanition with symptoms which are similar to those of beriberi. However, he thinks, that intoxication plays a part in the fatal result.

*In further support of the idea that the multiple neuritis of fowls subsisting on polished rice is due to inanition is the evidence supplied by those fowls that seemed to relish polished rice and ate their full daily allowance. As stated before, nearly all the birds fed on polished rice lost their appetite early in the experiment and would eat little or none of this grain, but a few were exceptions to the rule, notably numbers 5, 7, and 40, and they remained well for long periods of time. We are unable to reconcile our findings with the statement of Maurer<sup>(12)</sup> that those fowls which eat polished rice in the largest amounts are the first to become paralytic and that by feeding small amounts of the rice the sickness may be postponed for a long time.*

As shown in Table IV, out of the entire 56 fowls experimented with 27 developed neuritis, the average loss of weight up to the appearance of symptoms being 30.9 per cent. In every case but 2 (numbers 2 and 20) a loss greater than 21 per cent occurred before the symptoms developed. Of the 16 fowls which remained well throughout the experiments, only 5 lost weight at all and not one of these five decreased as much as 19 per cent. (Numbers 9, 14, 16, 27, and 33.) Only one fowl (number 40) gained when fed on polished rice and he was well at the end of 80 days when the experiment was concluded.

#### VI. BEARING OF THESE EXPERIMENTS ON THE ETIOLOGY OF BERIBERI.

As stated before, our original object in conducting these experiments was not to prove or disprove the identity of multiple neuritis in fowls and beriberi in man, but to test the neuritis-producing qualities, when fed to fowls, of certain native and imported rices and to use the information thus acquired as an aid in selecting the variety of grain and the degree of milling best suited for the Filipino troops. Nevertheless, as the work progressed, certain points of dissimilarity between beriberi and polyneuritis gallinarum became apparent and it may not be inappropriate to mention them here.

Fowls are especially susceptible to neuritis and get the disease under circumstances which have no effect on the nerves of some other animals. Monkeys, when fed on a diet of boiled, polished rice and water, remained well, although the experiments continued for more than three months. They had lost in weight and become weak, but did not show signs of

neuritis at any time. We can find in the literature no mention of neuritis in man having developed as a result of inanition among the professional "fasters" or among groups of men who were starving.

It would seem that the peripheral nerves of fowls are less resistant to degenerative influences than those of mammals and are among the first tissues to suffer when the animals are starved or given a deficient or ill-balanced diet. Our experience bears out the statement of Shibayama that polyneuritis of fowls occurs in cachectic animals, while beriberi is prone to appear among men previously well nourished.

Another point of difference is that œdema has been very rarely seen in fowls with neuritis<sup>(15)</sup> while it is common in beriberi in man. None of our fowls suffering from neuritis showed any œdema.

Therefore, we are inclined to join forces with those writers who consider that polyneuritis gallinarum and beriberi are not identical but we are fully in accord with Fraser and Stanton in their statements, (a) that its capacity for producing polyneuritis in fowls is an *accurate indicator* of the beriberi-producing quality of a rice and (b) that a low phosphorous content is a *reliable index* of the dangerous character of the grain. However, we have found that in neuritis-producing rice and in beriberi-producing dietaries the potassium is even more reduced than the phosphorus. The comparison between the two elements in rices is shown above in Table I. The diminution in phosphorus as compared with potassium in beriberi-producing diets was treated of in a former communication from the Board<sup>(10)</sup> and is referred to above in the discussion on polished rice combined with various salts (Table II). The latest work of Fraser and Stanton<sup>(22)</sup> seems to indicate that much the greater part (85 per cent) of the phosphorus in rice polishings is of no value in preventing polyneuritis of fowls. It now remains to be shown whether the real neuritis-preventing factor in polishings is the small per cent of phosphorus not yet accounted for, or the potassium, or some other element.

*The inference from the foregoing is that neuritis in fowls and beriberi in man is just as likely to be due to deficiency in salts of potassium as to deficiency in salts of phosphoric acid.* The results of our starvation experiments suggested that, as far as fowls are concerned, it might be a *deficiency of both phosphorus and potassium* which led to nerve deterioration. The experiments in classes 4, 5, 6, 7, and 8 indicated that adding to polished rice either phosphorus or potassium, or both elements, in two of their *common inorganic forms*, did not render the grain any safer as an exclusive article of diet for fowls. We are about to undertake another series of experiments combining with polished rice other mineral salts, such as potassium carbonate, potassium citrate, potassium phosphate, and magnesium phosphate.

## VII. CONCLUSIONS DRAWN FROM THE OBSERVATIONS.

1. Fowls develop multiple neuritis when fed exclusively on polished rice, whether Filipino Number 1 or Saigon choice rice is used.
2. Forcibly feeding polished rice to such fowls as have no appetite for it will not prevent the occurrence of neuritis.
3. Those fowls that voluntarily eat heartily of polished rice are able thereby to maintain their body weight and to defer or to prevent the development of multiple neuritis.
4. The administration of certain inorganic salts of phosphorus and of potassium, either alone or combined, to fowls subsisting on polished rice neither prevented multiple neuritis nor deferred its onset.
5. Fowls fed unhusked rice, *palay*, do not acquire multiple neuritis.
6. Fowls fed undermilled (unpolished) rice do not acquire the disease.
7. Whether the undermilled rice has a red or a yellowish-white pericarp is immaterial.
8. Fowls fed on undermilled rice combined with large amounts of sodium chloride do not develop multiple neuritis.
9. Fowls from which all food is withheld and only water allowed, develop multiple neuritis in some cases.
10. Fowls starved on reduced amounts of a neuritis-preventing undermilled rice acquire multiple neuritis in some cases.
11. Fowls kept entirely without food and those which are given all they will eat of polished rice lose weight with almost equal rapidity in the great majority of cases.
12. A loss of at least 21 per cent of the body weight almost invariably occurs before any signs of multiple neuritis become apparent.
13. The signs, symptoms, and nerve appearances are identical in neuritis produced by inanition and in that caused by feeding polished rice.
14. Spasticity is a late symptom in some fowls which develop neuritis and are then saved from death by the institution of mixed feeding.
15. In neuritis-producing rice and in beriberi-producing dietaries both the phosphorus and the potassium are markedly reduced in amount, the latter in greater degree than the former.
16. As an *index* of the beriberi-producing power of a given rice, reduction in the potassium content is probably quite as reliable as reduction in the phosphorus content.

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Group B: Under- milled rice.	Alone.	Filipino with yellow pericarp. Filipino with red pericarp, Subsistence Department.	9 10	4 4	0 0	----- -----	0 *1	----- 26	4 3	79 129.6	* Died of avian diphtheria.
	With salt.	Filipino (yellow) +0.36 gram* NaCl daily.	11	5	0	-----	*1	61	4	113.2	* On the 55th day this amount was doubled. * Died of avian diphtheria.
Group C: Unhusked rice.	Alone.	Filipino Macan rice (palay)-----	12	4	0	-----	0	-----	4	79	
Group D: Starvation.	Reduced amounts of a beriberi-pre- venting under- milled rice.	Filipino (yellow) 52 grams daily; $\frac{1}{4}$ usual allowance. <sup>b</sup>	13	1	1	107	122	0	-----	0	<sup>a</sup> After 43 days reduced to 26 grams and later (90th day) to 13 grams daily. <sup>b</sup> Mixed feeding instituted on the 115th day caused marked improvement of the general condition without apparent change in the neuritis.
		Filipino (yellow) 26 grams daily; $\frac{1}{4}$ usual allowance.	14	1	1	29	32	0	-----	0	
	Absolute.	Water only-----	15	8	3	14.3	17	5	12	0	<sup>c</sup> One fowl was saved by mixed feeding insti- tuted on the 23d day, and was chloroformed on the 55th day, another by mixed feeding on the 16th day and was chloroformed on the 27th day; the third died suddenly after mixed feeding begun the 16th day. Two of these very probably had neuritis, but as we were unable to save them by feeding mixed diet they are put in this column. Microscopically their nerves showed beginning degeneration.

TABLE IV.—*Individual numbers of fowls and percentages of weight gained or lost during experiments.*

Food			Individual number of fowl.	Weight at beginning.	Weight at appearance of signs of neuritis.	Percentages lost to appearance of signs.	Weight at end.	Percentage lost to end.	Percentage gained to end.	Developed polyneuritis.	Remained well.	Died of other disease.
				Gms.	Gms.		Gms.					
Group A: Polished rice.	Alone.	Class 1: Filipino No. 1.	*1	( <sup>b</sup> )			( <sup>b</sup> )					1
			2	1,190	1,077	9.5	885	25.7		1		
			3	1,077	623	42.2	566	47.5		1		
			4	1,133	700	38.3	623	45.1		1		
			20	1,218	1,034	15.2	828	32.1		1		
		Class 2: Saigon, Subsistence Department.	5	878	680	22.6	623	29.1		1		
			6	1,006	650	35.4	517	48.7		1		
			*7	1,162			1,020	12.3				1
			8	1,006	602	40.2	510	49.4		1		
		Class 3: Saigon 118 grams daily by force when necessary.	40	956			1,006		5.2		1	
			45	921	574	37.7	568	38.4		1		
			48	1,204	751	37.7	736	38.9		1		
			49	1,119	700	37.5	623	44.4		1		
	With various salts.	Class 4: 0.05 gram KCl daily.	21	1,112	865	22.3	722	35.1		1		
			22	1,218	914	25.0	744	39.0		1		
			23	1,268	864	31.9	637	49.8		1		
			24	970	650	33.0	474	51.2		1		
		Class 5: 0.03 gram H <sub>3</sub> PO <sub>4</sub> daily.	25	1,013	779	23.2	700	30.9		1		
			26	1,140	800	29.9	708	37.9		1		
			28	1,021	700	31.5	489	52.2		1		
		Class 6: 0.06 gram H <sub>3</sub> PO <sub>4</sub> daily.	59	1,226	970	20.9	871	29.0		1		
			60	1,176	830	29.5	807	31.4		1		
			*61	1,261			828	34.4				1
		Class 7: 0.05 gram KCl and 0.03 gram H <sub>3</sub> PO <sub>4</sub> daily.	29	1,091	857	21.5	687	37.1		1		
			*30	1,091			( <sup>b</sup> )					1
			31	1,091	779	28.6	700	35.9		1		
			32	1,070	566	47.2	538	49.8		1		
		Class 8: 0.03 gram H <sub>3</sub> PO <sub>4</sub> followed by 0.05 gram KCl daily.	*37	991			651	34.4				1
			27	1,098			998	9.2			1	

\* Died of avian diphtheria.

<sup>b</sup> Not known.<sup>c</sup> Found dead after a storm.

TABLE IV.—*Individual numbers of fowls and percentages of weight gained or lost during experiments—Continued.*

Food.			Individual number of fowl.	Weight at beginning.	Weight at appearance of signs of neuritis.	Percentage lost to appearance of signs.	Weight at end.	Percentage lost to end.	Percentage gained to end.	Developed polyneuritis.	Remained well.	Died of other disease.
Group B: Under-milled rice.	Alone.	Class 9: Filipino with yellow pericarp.	9	907			751	17.2			1	
			10	1,048			1,112		6.1		1	
			11	1,105			1,308		17.9		1	
			12	978			1,020		4.2		1	
		Class 10: Filipino with red pericarp, Subsistence Department.	38	1,176			1,445		22.8		1	
			39	921			1,176		27.6		1	
			*46	1,119			659	41.1				1
			47	1,042			1,431		37.3		1	
	With salt.	Class 11: Filipino (yellow) + 0.36 gram NaCl daily.	33	1,028			850	17.4			1	
			*34	1,155			850	26.5				1
			35	1,261			1,374		9.0		1	
			36	1,091			1,282		17.5		1	
			*58	871			715	18.0			*1	
Group C: Unhusked rice.	Alone.	Class 12: Filipino Macan rice ( <i>palay</i> ).	13	1,133			1,197		5.6		1	
			14	1,077			885	17.9			1	
			15	1,119			1,126		.6		1	
			16	907			736	18.9			1	
Group D: Starvation.	Reduced under-milled.	Class 13: ½ allowance.	18	1,006	538	46.6	510	49.4		1		
		Class 14: ½ allowance.	19	842	550	34.7	510	39.5		1		
	Absolute.	Class 15: Water only.	17	991	722	27.2	595	40.0		1		
			*41	793			481	39.4				1
			*42	963			524	45.6				1
			*43	907			566	37.6				1
			44	970	582	40.0	531	45.3		1		
			*54	907			637	29.8				1
			55	963	700	27.4	700	27.4		1		
			*56	991			550	44.6				1

\* Died of avian diphtheria.

\* Not known.

\* Found dead after a storm.

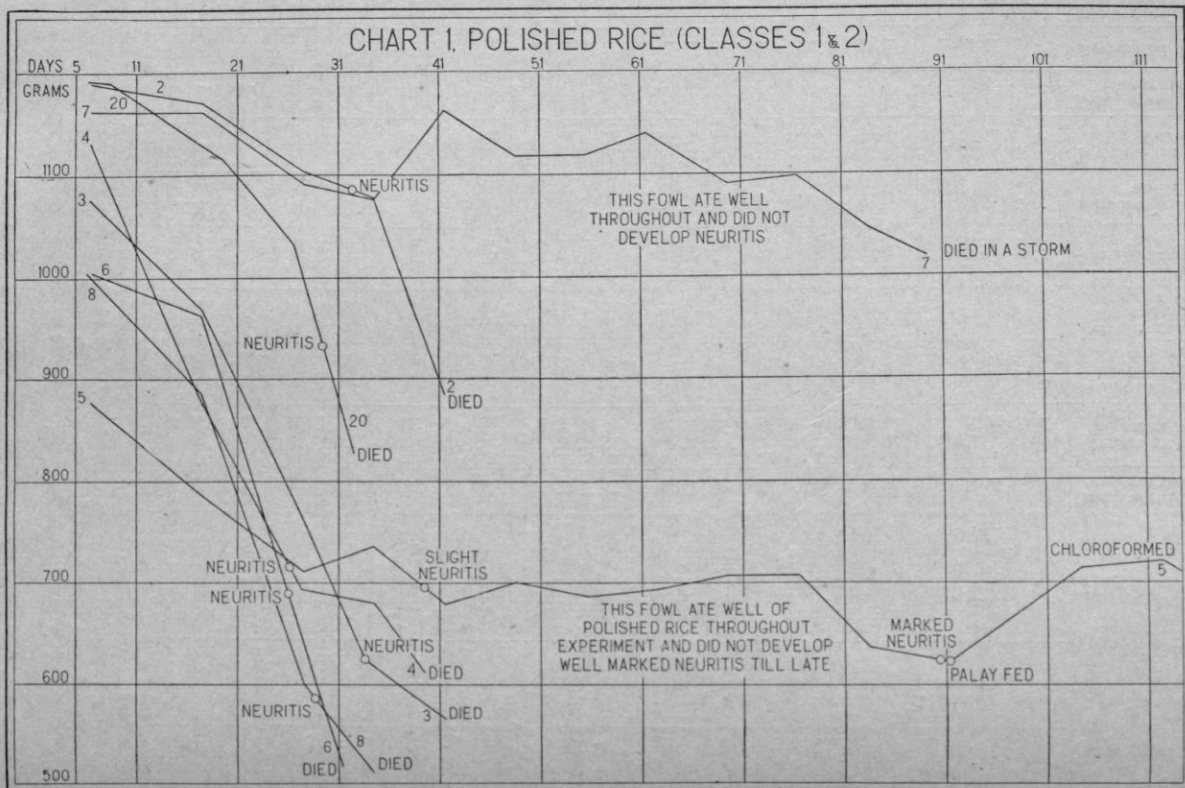
\* Sick with avian diphtheria.

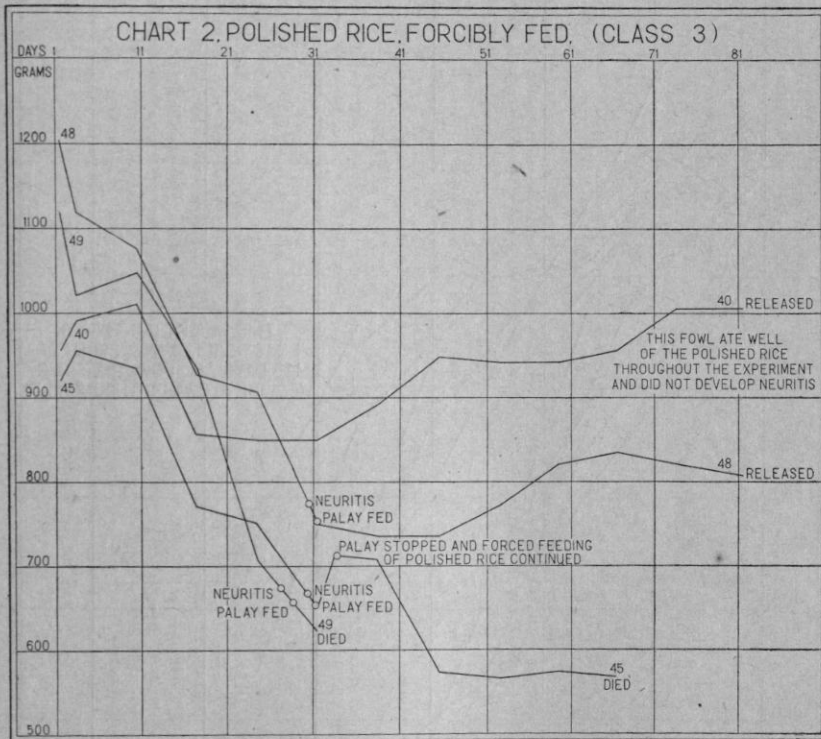
\* Recovered.

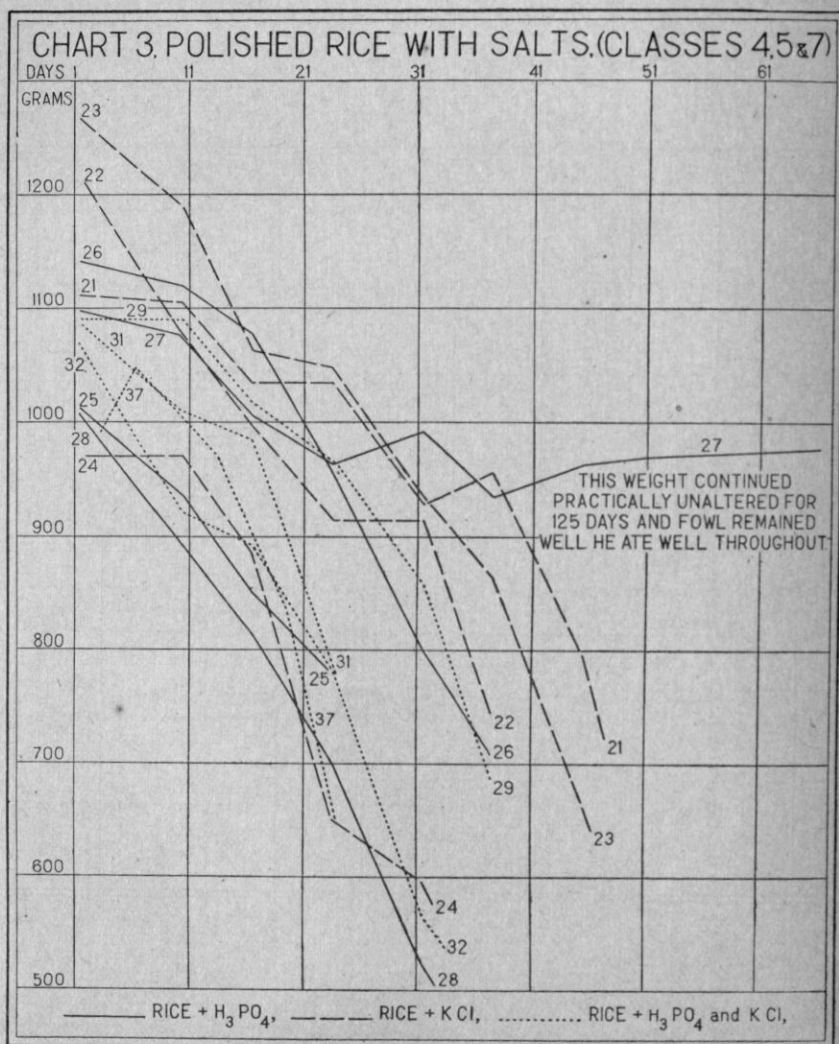
\* Died of starvation carried too far.

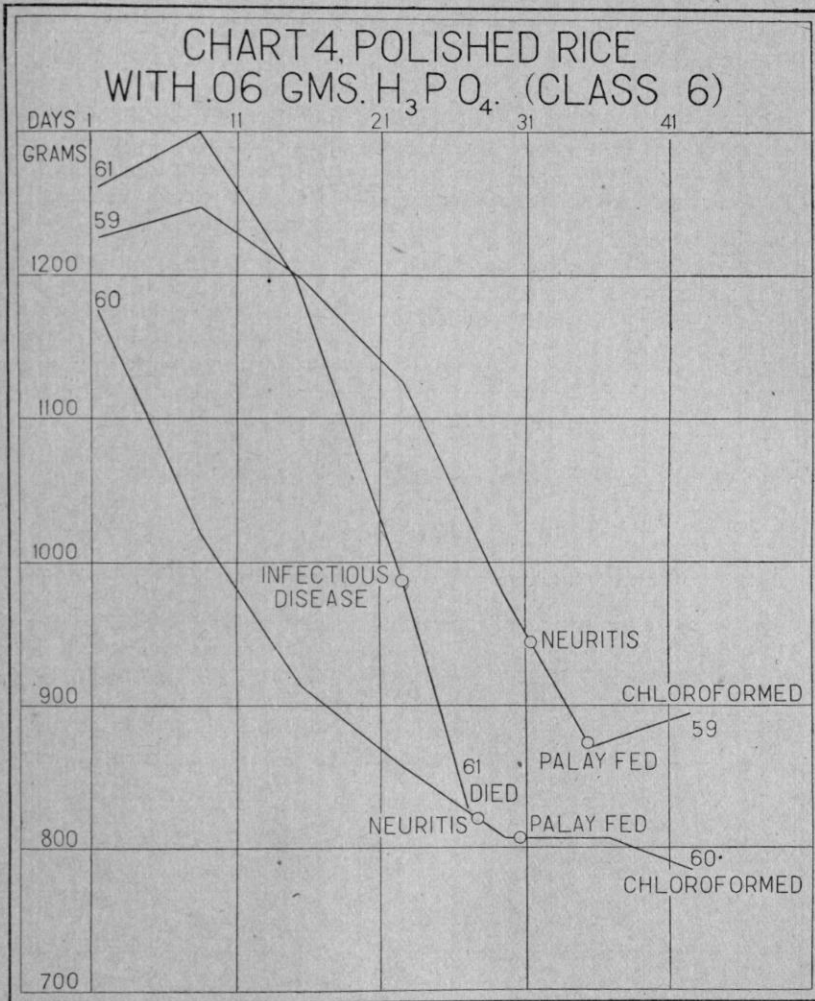
\* Cause of death unknown.

\* Died of starvation.

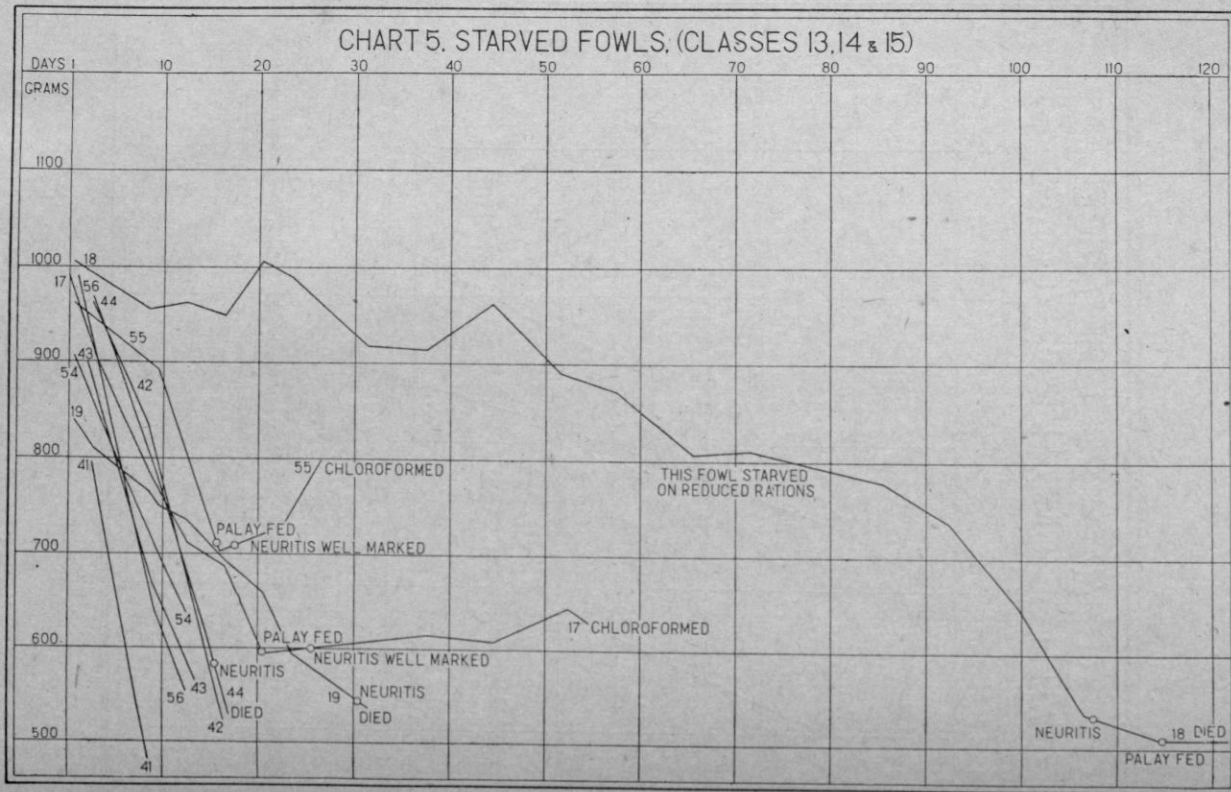








# CHART 5. STARVED FOWLS. (CLASSES 13, 14 & 15)



## ILLUSTRATIONS.

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### PLATE I.

- FIG. 1. Cages used for fowls during experiments.
2. Fowl number 5 in spastic stage. Shows extreme extension at knees and a tendency to teeter forward.
3. Fowl number 5 in spastic stage. Shows extreme extension at knees and a tendency to teeter forward.

### PLATE II.

- FIG. 4. Front view of fowl number 6 showing well-developed neuritis resulting from a diet of polished rice.
5. Profile view of fowl number 6 showing well-developed neuritis resulting from a diet of polished rice.
6. Fowl number 6. Late stage of neuritis resulting from a diet of polished rice.
7. Front view of fowl number 8 showing neuritis resulting from polished rice diet.

### PLATE III.

- FIG. 8. Profile view of fowl number 8 showing neuritis resulting from polished rice diet.
9. Front view of fowl number 18 which developed neuritis from starving on reduced rations. Shows wing-drop.
10. Profile view of fowl number 18. which developed neuritis from starving on reduced rations. Shows wing-drop and leg signs.
11. Front view of fowl number 17 showing late appearances in neuritis produced by starvation. Compare with Plate II, figure 4.

### PLATE IV.

- FIG. 12. Profile view of fowl number 17 showing late appearances in neuritis produced by starvation. Compare with Plate II, figure 5.
13. Front view of fowl number 55 showing early appearances in neuritis produced by starvation. Compare with Plate II, figure 4.
14. Profile view of fowl number 55 showing earliest appearances in neuritis produced by starvation.

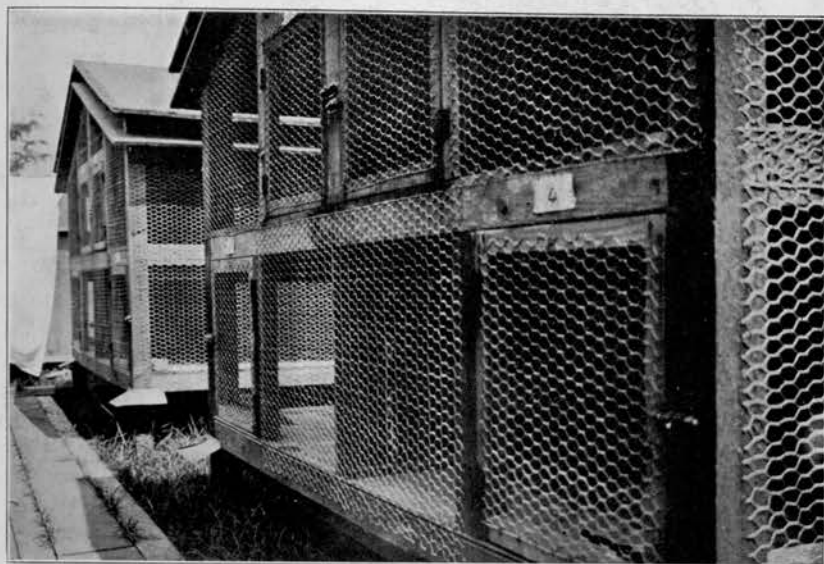


FIG. 1.—Cages used for fowls during experiments.

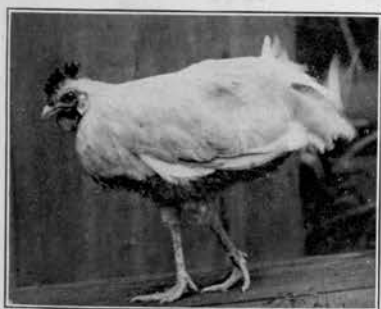


FIG. 2.—Fowl number 5 in spastic stage.  
Shows extreme extension at knees and  
a tendency to teeter forward.



FIG. 3.—Fowl number 5 in spastic stage.  
Shows extreme extension at knees and  
a tendency to teeter forward.

PLATE I.

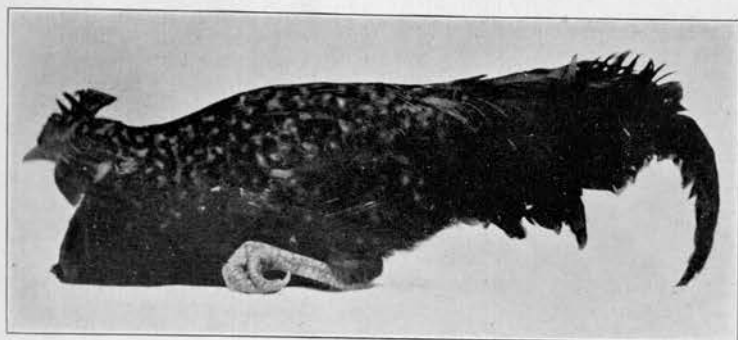


FIG. 5.—Profile view of fowl number 6 showing well-developed neuritis resulting from a diet of polished rice.



FIG. 6.—Fowl number 6. Late stage of neuritis resulting from a diet of polished rice.



FIG. 7.—Front view of fowl number 8 showing neuritis resulting from polished rice diet.



FIG. 4.—Front view of fowl number 6 showing well-developed neuritis resulting from a diet of polished rice.

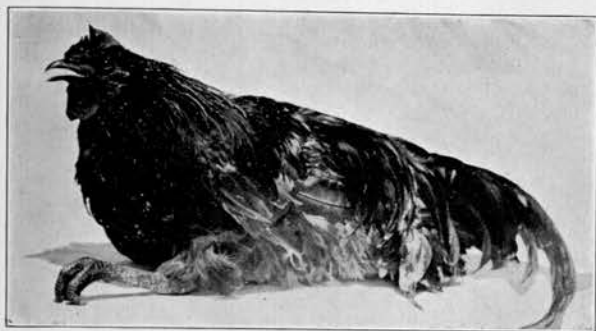


FIG. 8.—Profile view of fowl number 8 showing neuritis resulting from polished rice diet.



FIG. 9.—Front view of fowl number 18 which developed neuritis from starving on reduced rations. Shows wing-drop.

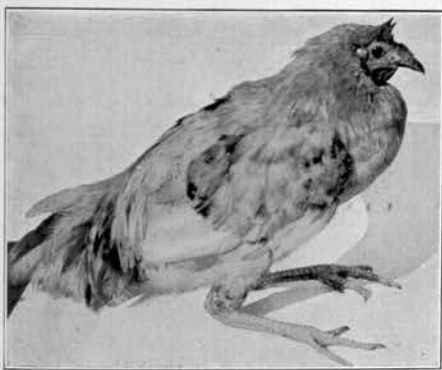


FIG. 10.—Profile view of fowl number 18 which developed neuritis from starving on reduced rations. Shows wing-drop and leg signs.



FIG. 11.—Front view of fowl number 17 showing late appearances in neuritis produced by starvation. Compare with Plate II, figure 4.

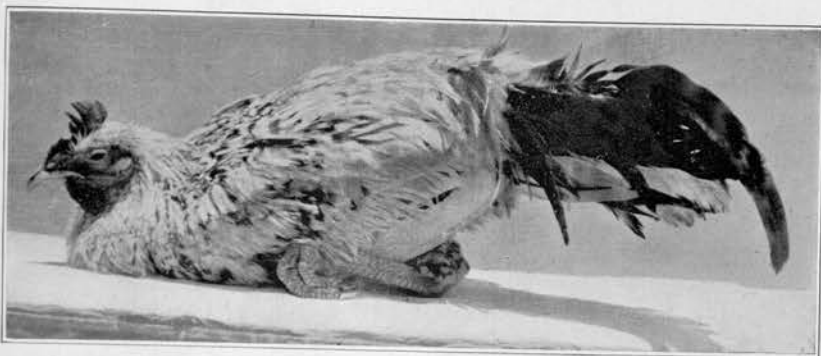


FIG. 12.—Profile view of fowl number 17 showing late appearances in neuritis produced by starvation. Compare with Plate II, figure 5.



FIG. 13.—Front view of fowl number 55 showing early appearances in neuritis produced by starvation. Compare with Plate II, figure 4.

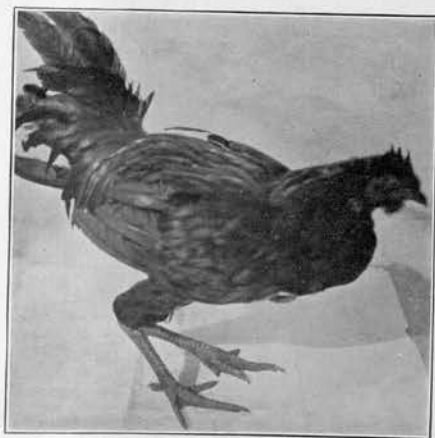


FIG. 14.—Profile view of fowl number 55 showing earliest appearances in neuritis produced by starvation.

PLATE IV.

## A STUDY OF THE INTESTINAL PARASITES FOUND IN CAVITE PROVINCE.<sup>1</sup>

By E. R. STITT.<sup>2</sup>

An out-patient department where medical aid has been given such Filipino patients as might present themselves, has been in operation during the year 1910 at the United States naval hospital, Cañacao, Cavite Province.

The 932 stool examinations upon which the statistics to follow are based, were therefore made upon specimens from cases of sick people and of these only such patients as it was thought required such an examination for diagnostic reasons were made to bring such a specimen of feces.

The patients presenting themselves at our clinic come almost exclusively from the city of Cavite and the adjacent towns of Caridad and San Roque. The conditions as regards rainfall and soil considerations are therefore the same for all of them. The rainfall in Cavite is slightly less than in Manila, where the yearly average approximates 75 inches. In this connection it should be stated that practically 80 per cent of the rain of the year falls in the months from June to October. Even after the most severe tropical rainfall the ground becomes dry in a very few hours. The average yearly temperature is about 27° C. and the difference between the average temperature of the coldest and hottest months is only about 4° C.

The towns of Cavite, San Roque, and Caridad are situated on a low-lying sandy peninsula, the soil being chiefly coarse-grained sand. Many of the lower levels are covered at high tide with salt water from the adjacent waters of Cañacao and Manila Bay.

These statements as to soil and climatic conditions are presented in view of a probable explanation of the small number of hookworm infections noted in our stool examinations.

Of the 932 examinations, 135 or 14.4 per cent failed to show the

<sup>1</sup>Read at the Eighth Annual Meeting of the Philippine Islands Medical Association, February 24, 1911.

<sup>2</sup>Surgeon, United States Navy, associate professor of medical zoölogy, Department of Tropical Medicine, College of Medicine and Surgery, University of the Philippines, Manila, P. I.

presence of intestinal parasites or their ova. The remaining positive examinations gave findings as follows:

Organism.	Number of infections.	Per cent.
<i>Ascaris</i> .....	627	67.2
<i>Trichocephalus</i> .....	607	65.1
Flagellates .....	135	14.4
Amœbæ .....	111	10.9
Hookworm .....	23	2.4
<i>Tenia saginata</i> .....	3	.8
<i>Balantidium</i> .....	1	.1
<i>Strongyloides</i> .....	1	.1

I personally, and very carefully, made the stool examinations in 100 of the above cases taken in sequence, using neutral red as well as with ordinary cover glass preparations, and obtained the following results:

Age.	Cases.	<i>Ascaris</i> .	Whip-worm.	Hook-worm.	Amœbæ.	Flagellates.
Under 5 years .....	42	37	28	0	2	2
5 to 10 years .....	27	25	23	0	2	5
10 to 25 years .....	16	9	14	1	2	1
25 to 50 years .....	10	8	4	0	2	1
Over 50 years .....	5	1	3	0	1	1
Total .....	100	80	72	1	9	10

Twelve of the cases tabulated above failed to show intestinal parasites or their ova. Of the entire total, positive for hookworm, 8 were between 5 and 15 years of age; 7 were between 25 and 35; 4 between 15 and 25; 3 over 35, and only 1 under 5 years.

Among the specimens positive for amœbæ there were organisms which as regards ectosarc characteristics and distribution of nuclear chromatin corresponded to *Entamoeba coli* and *Entamoeba histolytica*. Both types would frequently be observed in the same stool. Very few of these amœbic infections presented dysenteric or other symptoms. However, in three cases with marked anæmia and loss of energy and with the presence of very great numbers of amœbæ in the stools, ipecac treatment caused the disappearance of amœbæ and complete restoration to health.

We find, on comparing the percentage of cases positive for amœbæ with the results of examinations of the members of the Hospital Corps of the United States Navy on duty at this hospital, that an examination of the stools of 26 of these native-born Americans, in August, 1910, showed 34 per cent to be infected. A similar examination of 33 cases in December, 1910, gave positive findings for amœbæ in 37 per cent. There are certain points to be kept in mind in judging of the greater

frequency of amœbiasis in these members of the Naval Hospital Corps as compared with that in the Filipino patients examined.<sup>3</sup>

*First:* The stools of the men in the hospital corps were examined within a short time after being passed. It is a matter of common observation that a stool showing many amœbæ may, after standing for a few hours, fail to show the presence of a single amœba. Many of the specimens brought to the laboratory by Filipino patients were evidently many hours old.

*Second:* The expedient of giving a dose of salts prior to examination for amœbæ was not practicable with the Filipinos.

*Third:* Our experience has been that amœbæ are less frequent in young children and as about one-third of our Filipino patients were of such age, this should be taken into consideration.

At Bilibid Prison, Garrison encountered amœbic infection in 23 per cent of the cases.<sup>4</sup> In the medical survey of Taytay, his findings were 2.7 per cent.<sup>5</sup> Rissler and Gomez<sup>6</sup> report only 0.39 per cent of amœbic infection in their examinations in Las Piñas and no cases showing such infections in Tuguegarao and Santa Isabel. Such numbers are in striking contrast with those of former investigators, some of whom have reported as high a percentage of infection as 70.

Our findings as regards flagellates (14.4 per cent) correspond fairly closely with those of Garrison, namely, 21 per cent at Bilibid and 5.5 per cent at Taytay.

Repeated examinations with Giemsa staining and the counting of flagella in preparations in wet Gram solution showed only one species of flagellate to be present, *Trichomonas intestinalis*. *Lambliæ* was not found in a single instance.

Garrison, for *Trichocephalus* infection, obtained 59 per cent at Bilibid and 77 per cent at Taytay; Rissler and Gomez give 53 per cent at Las Piñas; 25.9 per cent at Tuguegarao, and 6.23 at Santa Isabel. Our findings were 65.1 per cent.

As regards *Ascaris* we found a higher rate of infection than for any other parasite (67.2 per cent). Garrison encountered 26 per cent at Bilibid and 82.9 per cent at Taytay. The percentages of Rissler and Gomez are 77, 73, and 60 respectively for Las Piñas, Tuguegarao, and Santa Isabel.

Garrison noted at Bilibid an incidence second only to *Trichocephalus* for hookworm infection, namely 52 per cent. His percentage of infection at Taytay was 11.6. Rissler and Gomez found 11.14 of all cases examined, infected with hookworms at Las Piñas; 8.01 per cent in Tuguegarao, and 45.38 per cent in Santa Isabel. We noted only 2.4 per cent for Cavite, San Roque, and Caridad.

<sup>3</sup>Thirty-five and six-tenths per cent as against 10.9 per cent for Filipinos.

<sup>4</sup>*This Journal*, Sec. B (1908), 3, 191.

<sup>5</sup>*Ibid.* (1909), 4, 257.

<sup>6</sup>*Ibid.* (1910), 5, 267.

The soil conditions mentioned above probably to a great extent account for the low incidence of hookworm disease as brought out in our examinations. Instead of a fine-grained, sandy soil which holds moisture tenaciously<sup>7</sup> we have here a coarse-grained sand which dries up completely almost as soon as the rain stops falling. Stiles attaches importance to the consideration that a wooded location is favorable to the development of hookworms because the shade of the trees counteracts the injurious effects of drying on the larvæ. There are practically no shade trees in this section. The frequent flooding of low-lying sections with sea water at the time of high tides must also influence the possibility of infection.

Our findings as regards *Strongyloides* (0.1 per cent) were far below those reported by Garrison at Bilibid (3 per cent) and at Taytay (0.7 per cent). Rissler and Gomez found 2.24 per cent infected in Las Piñas, but no cases were encountered in Tuguegarao and Santa Isabel. The same factors influencing hookworm infection in this locality may be operative for *Strongyloides*. Garrison found 0.2 per cent of the individuals examined at Taytay to be infected with ciliates, while Gomez and Rissler failed to find such infections at Tuguegarao or Santa Isabel. We found a single case in the 932 examinations.

Our three cases of tapeworm infection were with *Tania saginata*.

<sup>7</sup> Views of Nicholson and Rankin as to favorable soil for hookworm development.

# THE DYSENTERY BACILLUS WITH A BACTERIOLOGIC STUDY OF AN EPIDEMIC OF BACILLARY DYSENTERY IN THE PHILIPPINES.

By EUGENE R. WHITMORE.<sup>1</sup>

(From the Biological Laboratory, Bureau of Science, Manila, P. I.)

Shiga,<sup>(1)</sup> in 1908, announced that he had cultivated a special bacillus from the stools of dysentery patients and considered this bacillus to be the specific cause of bacillary dysentery. Since that time much attention has been given to the study of bacteria in the stools of patients suffering from dysentery.

In 1900, Flexner<sup>(2)</sup> and Strong<sup>(3)</sup> described a similar or identical bacillus in the stools of dysentery patients in Manila and almost at the same time Kruse<sup>(4)</sup> gave an account of a similar one in the same class of material in Germany. He rightly described the bacillus as non-flagellated, while Shiga called it a motile bacillus with flagella. From this time on the number of observations on the bacteria found in the stools of patients suffering with diarrhoea and dysentery increased very rapidly, and very soon workers began to note that there were differences between the bacteria isolated in various places, and between the bacteria isolated from different cases in the same place. Kruse considered his bacillus to be different from the Shiga-Flexner organism<sup>2</sup> because it was non-motile and without flagella.

Koch suggested that a commission should compare the various strains of the dysentery bacillus isolated by different men. This was done, and the Shiga, Flexner, Kruse, and two Döberitz strains were found to be morphologically and culturally alike. None of them bore flagella, while all of them showed a marked oscillating molecular motion. However, the Flexner strain did not agglutinate as strongly with the serum of a convalescent patient in the Döberitz epidemic as did the others.

Several observers, following this work, described dysentery-like bacilli which were found in various dysenteric conditions, especially in asylum dysentery. These organisms resembled the true bacilli of dysentery in cultures and in hanging drops, and they were agglutinated in as high dilutions of the serum of convalescent dysentery patients as were the true dysentery strains. However, staining showed them to have flagella, and further growth on different culture media proved them to be different from the true dysentery bacilli. From this it was evident that the serum of convalescent dysentery patients could not be used for the differentiation of dysentery and dysentery-like bacilli.

Martini and Lentz<sup>(5)</sup> immunized animals to two different strains of the

<sup>1</sup>Major, Medical Corps, United States Army; detailed to the Biological Laboratory, Bureau of Science, Manila, P. I.

<sup>2</sup>Flexner described his organism as a motile bacillus with flagella, while Strong was not able to demonstrate flagella.

dysentery bacillus and tested the agglutinating power of the different specific sera on the various strains. They also made a careful study of the morphology and cultural properties of the latter. They began by attempting to immunize rabbits and guinea pigs to seven strains, but so many animals died that they abandoned this method. Rabbits resisted one strain of the Flexner organism, and a good serum was obtained. Martini and Lentz then immunized a goat to the strain "Shiga," and prepared a very active serum.

They were able to show from the agglutination reactions with these sera that the Shiga, Kruse, and eight other strains were identical (Group I), while the Flexner and Strong strains from the Philippines differed from the latter (Group II). It was further proved that one of Strong's strains differed from the Flexner in its agglutinability, although Martini and Lentz do not seem to have made it into a separate group at that time, but left it with the Flexner, pseudodysentery (Kruse), and several others, all of which were different from the Shiga and Kruse types.

Hiss and Russell(6) described a bacillus which they isolated from a fatal case of diarrhœa in a child. They called this organism "Bacillus dysenteriae Y" and it soon was shown that the bacillus of asylum dysentery was identical with this variety.

It does not appear that Martini and Lentz tested the agglutinability of bacillus Y to their "Flexner" serum, although they seem to have had it in their series (Pseudodysentery Kruse) and found that it did not agglutinate with their Shiga serum. Since we know now that the serum from the Flexner organism often agglutinates Bacillus Y in as high dilution as it does the Flexner, it would have been interesting to have studied this question.

Hiss and Russell differentiated their Bacillus Y from the Shiga bacillus by means of mannite- and maltose-litmus agar, and almost at the same time Lentz(7) used these same media for the differentiation of dysentery and dysentery-like bacilli. He worked with the strains which Martini and Lentz had used in their agglutination experiments. By means of the sugar media, he was able to show that one of Strong's strains was different from that of Shiga and Flexner, while the two latter were also proved to be different from each other by their behavior in the sugar media. This corresponded to the finding of Martini and Lentz, as a result of their studies of the agglutination reactions of the same three strains.

This brief review of the literature shows that the dysentery bacillus had been divided into four groups by the use of sugar media and that three of these groups were also distinct in their agglutinability.

The following table gives the cultural differences in sugar media that are relied upon for isolation of the dysentery bacillus and to separate it into types:

*Cultural differences in sugar media.*

Litmus agar with addition of—	Appearance in culture of bacillus.			
	Shiga-Kruse.	Y.	Flexner.	Strong.
Lactose.....	Blue.	Blue.	Blue.	Blue.
Dextrose.....	Red.	Red.	Red.	Red.
Mannite.....	Blue.	Red.	Red.	Red.
Maltose.....	Blue.	Blue.	Red.	Blue.
Saccharose.....	Blue.	Blue.	Blue.	Red.

Three of these types (Shiga, Flexner, and Strong) correspond exactly to the agglutination reactions, while the other one (Bacillus Y) is only irregularly differentiated from that of Flexner by that reaction. Furthermore, the action on mannite corresponds to a difference in toxicity; the Shiga-Kruse type which does not *produce acid in mannite*, is very toxic for animals, while the other types which *produce acid in mannite* are not nearly as toxic. This difference in toxicity was clearly shown by Martini and Lentz at the time they differentiated their two groups on the basis of the agglutination reactions.

A number of other types have been added at times, and the above have been separated into a number of others by various workers. Thus Shiga(8) made a fifth type which differed from the "Flexner" in that it produced acid in mannite in the first twenty-four hours, and then alkali. It was very close or similar to the Flexner type in all other properties, including agglutinability. Ohno(9) grew a large number of strains of the dysentery bacillus in the sugars for fourteen days and in this way divided the dysentery bacillus into 15 varieties because of their action on the sugars; but when he tested the agglutinability of his various strains he did not observe these varieties.

Iletsch(10) already had pointed out that the reaction differed somewhat according to the percentage of sugar in the medium. In addition to sugar, the media contain peptone and albumoses, and while the decomposition products of the sugars are mainly acid, those of the peptone and albumoses are mainly alkaline. The bacteria attack both classes of substances and upon the amount of one or the other present, as well as the avidity with which one or the other is attacked, depends the acidity or alkalinity of the sum total of the products of decomposition. Again, an organism may change in its relative avidity for the carbohydrate and the proteid content of the medium. Hiss and Russell(6) and a number of others have shown that an organism may change in its action on sugars after it has been on artificial media for some time.

Finally, the absorption experiment of Castellani has been used for the separation of the dysentery bacillus into types, but it gives so many that it almost hopelessly complicates the placing of any particular strain.

During an epidemic of bacillary dysentery in the Philippines occurring in the summer of 1909, I was able to isolate dysentery and dysentery-like bacilli from the stools of a number of cases, and I proceeded to study the organisms along the lines indicated in the foregoing review of the literature. In isolating the organisms, I tried the various lactose-agar media, but did not find any of them to be superior to the litmus-lactose-agar for practical work on the dysentery bacillus.

I prepared my plates in the laboratory in Manila, took them with me into the provinces where the dysentery was most active, streaked the plates there and then brought them back to the laboratory with me, or else, when I remained in the provinces for a few days, I picked colonies and transplanted them into tubes before coming back. In this way I was able to isolate a bacillus of the Shiga-Kruse type from 12 out of 40 cases of severe, acute dysentery in natives of two towns of Batangas Province where there was an epidemic of acute dysentery with a high

mortality.<sup>3</sup> No other strain of the dysentery bacillus was found by me in that locality. I was able four times to isolate a bacillus of the Flexner-Strong type and one of the Shiga-Kruse type once from sporadic cases of acute dysentery around Manila. Besides this, I obtained a large number of dysentery-like bacilli.

These organisms were determined by the cultural characteristics, including their reactions in sugar media, their pathogenicity for lower animals, and their agglutination reactions with sera of animals immunized to known strains of the various types of the dysentery bacillus. As all but one of the strains of the Shiga-Kruse type came from one locality and all of them were identical, I chose the Manila strain (P. S. II) and one of the Batangas strains (P. S. I). In the same way I selected two of the Flexner-Strong strains (P. A. I. and P. A. II) and six of the dysentery-like organisms (L. I. to L. VI). As my further work in agglutination reactions was to immunize animals to each strain and then to test the agglutinability of every strain with every serum, it was manifestly necessary for me to keep the number within working limits, and there was no necessity of working with a large series that culturally and by agglutination reactions had been shown to be identical. Again, reasonable economy in animals required that I should not use too many strains, especially as I was working with rabbits, and my Shiga-Kruse strains were so virulent for them that I lost a number of animals before I prepared a serum that agglutinated in sufficiently high dilution to be of any value.<sup>4</sup>

The following chart gives the morphology and cultural character of the strains chosen by me for further work, as well as two of the Shiga-Kruse type (S. S. I and S. S. II) and one of the Flexner (S. A. II), kindly sent to me by Professor Shiga, and one strain of the Flexner-Strong type (S. A. I) brought from Heidelberg by Doctor Coca.

I also tried Jehle and Charleton's(11) serum medium with the sugars. The result was entirely in accord with the findings on agar.

From the following chart it can be seen that the first four strains fall in the Shiga-Kruse type, while the next four belong to that of Flexner-Strong. The last six easily are shown not to be dysentery bacilli at all. There is no example of the Bacillus Y.

<sup>3</sup>I took blood from each patient for agglutination tests, at the time that I obtained the stool. The blood-sera of patients who had been sick less than three days did not agglutinate the dysentery organisms; the sera from those who had been ill three to five days agglutinated slightly, or not at all, while that from patients who had been ill over five days agglutinated from 1:40 to 1:100, but no special work was done in this line, as the patients' sera were not depended upon at all for determining the organisms.

<sup>4</sup>Martini and Lentz say that the serum should agglutinate in a 1:300 dilution.

CHART A.

Culture.	Size and form.	Motility.	Flagella.	Indol production.	Properties of growth on—								
					Plain agar.	Litmus-lactose-agar.	Litmus-dextrose-agar.	Litmus-mannite-agar.	Litmus-maltose-agar.	Litmus-arose-agar.	Litmus milk.	Bouillon.	
P. S. I.	Short plump bacillus.	Marked molecular motion.			White, spreading slightly.	No change.	Acid.	Alkaline.	Alkaline.	Alkaline.	Slightly acid, not coagulated.	Cloudy, with tendency to settle.	
P. S. II.	do.				do.	do.	do.	do.	do.	do.	do.	No scum on top.	
S. S. I.	do.				do.	do.	do.	do.	do.	do.	do.	Do.	
S. I. II.	do.				do.	do.	do.	do.	do.	do.	do.	Do.	
P. A. I.	do.			Trace.		do.	do.	do.	Acid.	Acid.	do.	do.	Do.
P. A. II.	do.					do.	do.	do.	do.	do.	do.	do.	Do.
S. A. I.	do.					do.	do.	do.	do.	do.	do.	do.	Do.
A. A. II.	do.			Trace.		do.	do.	do.	do.	do.	do.	do.	Do.
L. I.	do.					Yellowish after 3 days.	do.	Acid, decoloration at bottom.	Alkaline.	Alkaline.	do.	Alkaline, not coagulated.	Heavy sediment.
L. II.	do.					Like P. A. I.	do.	Acid.	Acid slight.	Acid.	No change.	do.	Like P. A. I.
L. III.	Longer than above.					Richer growth.	do.	do.	Alkaline.	Alkaline.	Alkaline.	do.	Rich growth, heavy sediment.
E. IV.	Short plump bacillus.					Like P. A. I.	do.	Acid slight.	do.	Acid.	do.	do.	Like P. A. I.
L. V.	Longer than above.			Slight.		Rich growth white.	do.	Acid, decoloration at bottom.	No change.	Decolorized.	No change.	Decolorized, not coagulated.	Heavy sediment, scum on top.
L. VI.	do.			Slight.		do.	do.	do.	do.	do.	do.	do.	Do.

\* Became slightly acid after six weeks.

Using the four Shiga-Kruse strains, I attempted to determine their type according to Ohno's method. Two of my strains (P. S. I and P. S. II) were isolated recently, while two (S. S. I and S. S. II) had been on artificial media for some time. All of the four belonged in Ohno's type A. Eight months later I tested these same strains again. One (P. S. II) had changed to Ohno's type B, while the other three remained in his type A.

I used rabbits for the preparation of specific sera and made all injections intravenously. The animals were weighed once a week and the injections were given as closely as possible within the same interval, consideration being given to the weight and general conditions of the animal.

The first four or five injections were of organisms grown in agar for 18 hours and heated to 60° for one hour, while the later ones were of living organisms. Each animal usually received fourteen injections. The first was always very small and later the dose gradually was increased. I had great difficulty with the rabbits which were given the Shiga-Kruse cultures, 1/50 of a loop of a killed culture of one of the recently isolated strains killing rabbits when injected intravenously. I lost animals from the use of these strains as late as the fourteenth injection. The two strains received from Japan were not so virulent, possibly because they had been on artificial media for some time. The animals withstood larger doses of the latter and this may account for the fact that I attained sera with stronger agglutination from them. These facts appear in the agglutination tables given below. No especial difficulty was encountered in giving the Flexner strains and non-dysentery organisms in much larger doses than is possible with the Shiga-Kruse strains.<sup>5</sup>

The animals were bled about ten days after the last injection. In order to obtain the large amount of serum needed for this work and still not to kill the rabbit, the following method was used:

A large test tube was provided with a rubber stopper having two perforations. A piece of glass tubing connected by a short piece of rubber tubing to a long, slender aspirating needle passed through one perforation; a piece of glass tubing through the other, the latter connected with the vacuum apparatus by a long piece of rubber tubing. The rabbit was placed on its back on an animal board,

<sup>5</sup> At the same time I immunized a horse to both Shiga-Kruse and Flexner types, by giving weekly intravenous injections of living organisms alternating with the filtrate from an old culture in alkali bouillon. One horse died of an intercurrent condition after it had received ten injections, but another received seventeen injections and at the end of that time his blood agglutinated Shiga at 1:800 and Flexner above 1:1000. The animal was bled ten days after the last injection and the serum put up for use in the treatment of bacillary dysentery. So far we have had very little opportunity to try it, as the epidemic dysentery under discussion was over by the time the serum was ready for use.





TABLE IV.

[illegible]

TABLE V.

[illegible]



TABLE VIII.

[illegible]

TABLE IX.

[illegible]

TABLE X.

Culture.	Is agglutinated in rabbit serum L. I in a dilution of —										
	1:10.	1:20.	1:50.	1:100.	1:200.	1:300.	1:400.	1:500.	1:600.	1:700.	1:800.
P. S. I .....	—	—	—	—	—	—	—	—	—	—	—
P. S. II .....	—	—	—	—	—	—	—	—	—	—	—
S. S. I .....	—	—	—	—	—	—	—	—	—	—	—
S. S. II .....	—	—	—	—	—	—	—	—	—	—	—
P. A. I .....	+	—	—	—	—	—	—	—	—	—	—
P. A. II .....	±	—	—	—	—	—	—	—	—	—	—
S. A. I .....	±	—	—	—	—	—	—	—	—	—	—
S. A. II .....	±	±	—	—	—	—	—	—	—	—	—
L. I .....	+	+	+	+	+	+	+	+	+	+	±
L. II .....	±	—	—	—	—	—	—	—	—	—	—
L. III .....	—	—	—	—	—	—	—	—	—	—	—
L. IV .....	+	—	—	—	—	—	—	—	—	—	—
L. V .....	+	—	—	—	—	—	—	—	—	—	—
L. VI .....	+	—	—	—	—	—	—	—	—	—	—

From the foregoing tables it is evident that the first four strains are identical; also that the next four are identical among themselves, but are entirely different from the first four. Two of the first four strains (S. S. I and S. S. II) are known to be of the Shiga-Kruse variety, while two of the next four (S. A. I and S. A. II) are Flexner strains.

I was interested in finding that non-dysentery strains L. V and L. VI were both agglutinated in a dilution above 1:1,000 of serum L. V and serum L. VI. On checking them, I found that L. V and L. VI both came from the same patient and that, owing to an error in the spelling of the name, two stools from the same patient had been examined as coming from different ones.

## SUMMARY.

1. In an epidemic of bacillary dysentery with a high death rate in Luzon, Province of Batangas, P. I., it has been shown that the Shiga-Kruse type of dysentery bacillus was the causative agent.

2. At the same time, the Flexner-Strong type of dysentery bacillus was found in some cases of dysentery around Manila.

3. The Bacillus Y and the Strong type with which Leutz worked were not found.

4. Great care is necessary in describing types of the dysentery bacillus from their reactions in sugar media alone, as the amount of sugar present and the length of time the organism has been on artificial media often affect the reaction.

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- (7) LENTZ. *Ibid.*, 559.
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\*The excellent article by Lentz in Kolle & Wassermann's *Handbuch d. Path. Mikroörg.* (1909), Erg. Bd. II, p. 391, gives a full discussion and a full bibliography on the subject.

## PRACTICAL EXPERIENCES WITH BERIBERI AND UNPOLISHED RICE IN THE PHILIPPINES.<sup>1</sup>

By VICTOR G. HEISER.<sup>2</sup>

The advances made during the past year in placing the etiology of beriberi upon a scientific basis have now proceeded sufficiently to warrant the inference that prophylactic medicine has the knowledge at its command to place this scourge among the preventable diseases.

While it has been possible to control outbreaks of beriberi in public institutions in the Philippines during the past ten years by reducing the rice in the diet and replacing it with meat, vegetables, mongos,<sup>3</sup> etc., yet it was not until the papers which were read at the last annual meeting of the Far Eastern Association of Tropical Medicine, especially those of Fraser<sup>4</sup> and of Aron<sup>5</sup> gave the clue, that a rational method for the prevention and cure of the disease became available.

Briefly, it will be remembered that these gentlemen showed by experimental data that beriberi in man and polyneuritis in fowls could be caused by using as the staple article of diet, rice, from which the outer portion or pericarp had been removed, and that, unless advanced degeneration of the nerves had occurred an immediate amelioration of the symptoms took place when rice with the pericarp, or its equivalent, was substituted.

Numerous analyses of rice sold in the Manila market have been made by Aron, and these soon proved that Saigon rice number 2, as well as

<sup>1</sup>Read at the Eighth Annual Meeting of the Philippine Islands Medical Association, February 23, 1911.

<sup>2</sup>Passed assistant surgeon, United States Public Health and Marine-Hospital Service; Director of Health for the Philippine Islands; and professor of hygiene, College of Physicians and Surgeons, University of the Philippines.

<sup>3</sup>A small bean, *Phaseolus radiatus* Linn. (*P. mungo* Blanco), similar to *katjang idjo* of Dutch East India. It has been proved by the native physicians of the Philippines as valuable as *katjang idjo* as a popular remedy for beriberi. According to the analysis of Aron (*This Journal*, Sec. B (1910), 5, 88) this bean contains 23.75 per cent protein; 9.56 per cent water; 0.77 per cent  $P_2O_5$ ; 4.5 per cent fat; 6.4 per cent crude fiber.

<sup>4</sup>*Ibid.*, 55.

<sup>5</sup>*Ibid.*, 81.

locally polished rice, almost invariably contained less than 0.4 per cent of phosphorus pentoxide, unpolished or slightly polished rice was found to contain from 0.5 per cent to 0.75 per cent of phosphorus pentoxide.<sup>9</sup>

Since the opening of the Culion leper colony in 1906, rice has been the staple article of diet in the place, and it was customary to use either Saigon rice number 2, or local polished rice. Beriberi was more or less continuously present in the colony until February, 1910. By substituting meat and mongos for rice it was always possible to reduce the number of cases of beriberi, but the disease was never completely eradicated. It was found later that this failure was probably due to the fact that many of the lepers preferred to deny themselves food rather than to eat mongos, so that we had starvation as well as improper diet to deal with.

The total number of deaths at Culion by months from February, 1909, to February, 1910, among an average population of 1,537 was as follows: February, 39; March, 54; April, 52; May, 47; June, 48; July, 57; August, 61; September, 65; October, 43; November, 80; December, 188; January, 164; a total of 898. Of this number 309 were due to beriberi.

In February, 1910, the use of unpolished rice was made compulsory for all inmates of the Culion leper colony.

The total number of deaths for the months from February, 1910, to February, 1911, among an average population of 1,952, or a population greater by 27 per cent, was as follows: February, 66; March, 36; April, 29; May, 22; June, 27; July, 15; August, 24; September, 12; October, 13; November, 15; December, 58; January, 52; or a total of 369.

The increased death rate in December and January was due to an acute outbreak of bacillary dysentery. Of the number cited, there were no deaths from beriberi after February, 1910.

At the end of January, 1910, there were approximately 50 cases of beriberi undergoing treatment in the Culion hospital. Upon the suggestion of Doctor Aron, 30 grams of rice polishings mixed with milk and sugar were given to these patients twice daily. With the exception of two very advanced cases that died within a few days after this treatment was begun, all of them were able to leave the hospital, and within four weeks every case of beriberi was reported as cured by the attending physician of the hospital. So much for Culion.

Prior to May, 1910, beriberi was very common throughout the Philippines, in jails, light-house stations, charitable institutions, on Government vessels, and among the Philippine troops of the United States

<sup>9</sup>I wish to make clear that the amount of phosphorus in rice is only given because it is a ready method for determining the degree of polishing that a given rice has undergone; in other words, the estimation of the amount of phosphorus is a laboratory method of ascertaining whether much or little of the pericarp has been removed and at this time it can not be said that the lack of phosphorus causes beriberi.

Army. An investigation of these has shown that it was the invariable practice to use polished rice as the staple article of diet in all of the places mentioned. In May, 1910, an Executive Order was issued by the Governor-General of the Philippine Islands prohibiting the use of polished rice in all public civil institutions. Since August, 1910, only two cases of beriberi in the above places have come to the attention of the writer. One of these was among the crew of the steamer *Rizal*. An inspection of the ship's stores showed that the rice was of the white polished variety. Further inquiry elicited the fact that it was customary for the crew of this vessel to use a varied diet which may account for the fact that there were not more cases. The other case occurred in a prisoner in the jail at Tacloban. The physician in charge reported that it had not been possible to purchase unpolished rice at Tacloban and for that reason polished rice was being used. He added that every effort was, however, being made to comply with the spirit of the Executive Order by using more meat, mongos, potatoes, green vegetables, and fish.

At the Hospicio de San José, which is an insane and orphan asylum of over 700 inmates, beriberi has almost constantly been present, at least during the past ten years. Since June, 1910, unpolished rice has been used, and a few weeks after its use was begun beriberi disappeared, and since that time no further cases have been reported.

Extensive inquiry made throughout the Philippine Islands has almost invariably shown that in districts in which hand-pounded, or, in other words, unpolished rice, is commonly used, there is little if any beriberi, whereas in districts in which machined, or, in other words, polished rice, is served as the staple article of diet, beriberi is quite common. However, an apparent exception to this general rule is found among the residents of the Batanes Islands. It may perhaps be mentioned that these are isolated islands north of Luzon and south of Formosa, which have communication with the outer world only a few times each year, and, owing to their inaccessibility, they generally escape visitations of cholera and other dangerous communicable diseases.

The Batanes are poorly adapted to rice culture, and for this reason a considerable amount of polished rice is imported each year, and it would seem reasonable to infer that if the present theories with regard to the etiology of beriberi are correct, cases of this disease should be encountered in these islands. However, an investigation of the dietary of the inhabitants of the Batanes Islands shows that meat and potatoes are more commonly used than in other parts of the Philippines. In brief, food of various kinds, other than rice, is so plentiful that rice is not the staple article of diet to the same extent as elsewhere in the Archipelago.

Considerable difficulty has been encountered and much opposition has

resulted from the attempt to introduce unpolished rice. When the Army and the Insular Government entered the market to purchase large quantities, it developed that rice dealers were unable to supply the demand because managers of rice mills refused to adjust their process of manufacture to meet the new requirements. This resulted in the use of large quantities of rice that came from the mills immediately after it was husked. The machines that are employed locally for this purpose allow many of the smaller rice grains to pass through without the husks being removed from them. Previously such rice went directly to the polishing machine which not only polished the grains but the husks were also removed from such as still retained them, so that the finished product was clean. It was apparent then that much of unpolished rice which was issued in the beginning was not very clean and contained many husks. This gave rise to much complaint among those who were required to use it. It was frequently alleged that the husks tickled their throats and often caused gastritis. Upon investigation no reliable evidence as to the gastritis could be obtained. Commissary officers, prison wardens, and others who were directly charged with carrying out the orders to use unpolished rice were constantly besieged with complaints, and it was but natural that they should take the course of least resistance and recommend that its use be discontinued. To add to the difficulties of those who were insisting upon the use of unpolished rice, the rumor spread that the latter, when stored in bulk, soon spoiled, thus causing great financial loss. Investigation of this matter showed that there was no reason to believe that unpolished rice when stored under the same conditions as polished rice spoiled any more rapidly.

A campaign of education was then begun. Doctor Aron frequently went to the rice mills in person and was invariably able to demonstrate that rice could be rendered clean and free from husks without polishing it to a degree that would be harmful. Similar work, with like results, was accomplished by Hight in Siam, so that it may now be said that clean unpolished rice, satisfactory in appearance, can be obtained in the Philippines and abroad, and that the original objections to its use no longer exist.

By January, 1911, so much evidence had accumulated showing unpolished rice to be an important factor in the prevention of beriberi that it was deemed most desirable to bring about its general use in the Philippines for a few years at least, in order to test the theory thoroughly. At the most no harm can result, and upon the other hand every promise was held out that many hundreds of lives could be saved and a still greater morbidity avoided. Experimental investigations made by Doctor Aron showed that a rice which has only been polished to a point where it still contains 0.4 per cent of phosphorus pentoxide may be regarded as incapable of producing beriberi. Almost at the same

time similar conclusions were announced by Highet. Therefore, for purposes of convenience a rice containing less than 0.4 per cent of phosphorus pentoxide is regarded as polished and that which contains a greater percentage of phosphorus pentoxide as unpolished rice.

Accordingly, a bill was drafted which had for its purpose the bringing about of the general use of unpolished rice in those quarters where it furnished the staple article of diet. After considerable discussion with physicians, lawyers, legislators, and others, it was deemed advisable to attempt to secure the desired result by a law that would impose a tax of 5 centavos (2.5 cents United States currency) per kilogram upon all polished rice sold, whether it be foreign or domestic. However, owing to the fact that the Legislature adjourned during the early days of February, there was not sufficient time to present this matter to both Houses.

Because of the successful experience with unpolished rice in the prophylaxis of beriberi in the Philippines during the year, and since these data confirm the work of Fraser and Stanton,<sup>7</sup> Aron,<sup>8</sup> Kilbourne,<sup>9</sup> de Haan,<sup>10</sup> and Highet,<sup>11</sup> as reported at the last annual meeting of the Far Eastern Association of Tropical Medicine, it is believed that the time has come for the medical profession to aid in completing the last step in the test which promises so well to place another weapon in the hands of prophylactic medicine for the eradication of another of the world's serious and costly diseases.

<sup>7</sup> *Loc. cit.*

<sup>8</sup> *Loc. cit.*

<sup>9</sup> *This Journal, Sec. B* (1910), 5, 127.

<sup>10</sup> *Ibid.*, 65.

<sup>11</sup> *Ibid.*, 73.

## PERINEAL LITHOLAPAXY (KEITH'S OPERATION).

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(Rajkot, India.)

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The trend of general surgical opinion, with reference to the treatment of stone in the urinary bladder, is, I suppose, more and more in favor of the employment of crushing operations in almost all cases in which they are practicable, and while admitting that very large stones usually are best dealt with by suprapubic lithotomy, and that certain cases associated with cystitis or suppuration about the neck of the bladder derive benefit from the drainage which is most easily afforded by a perineal lithotomy, I take it that everyone will agree that any safe procedure which enables litholapaxy to be applied to stones which would otherwise have to be removed by serious cutting operations is worthy of consideration. Keith's operation has this application, and it is with the view of bringing it to the notice of surgeons who perhaps may not previously have heard of it that this short account has been written.

It may first be noted that several procedures involving a combination of crushing with a larger or smaller incision in the perineum have from time to time been advocated by various authorities. Dolbeau was the first surgeon, so far as I am aware, to publish an account of such a combined operation, but his operation, which in essentials is that still described in the text-books under the name of perineal lithotomy or litholapaxy, differs from Keith's in the important fact that a much larger opening is made in the urethra to allow of the passage of large instruments designed merely to break up the calculus roughly, and not to crush it completely; and, indeed, it may be said that this method has more in common with lithotomy than litholapaxy pure and simple. Dolbeau's operation apparently was practiced intermittently by various surgeons for many years, but it was not until Dr. Keith of the Indian Medical Service introduced his modification that any large number of cases of crushing through a perineal incision were published, and that the operation—so changed in its details as to be practically new—acquired almost all the advantages of an uncomplicated litholapaxy. Dr. Keith, in his capacity of Civil Surgeon of Hyderabad, Scinde, with its five hundred cases of stone a year, had unrivaled opportunities of demonstrating the value of the procedure, and recorded a series of fifty-three cases in men, with three deaths, and one hundred and six cases in children, with no deaths. Surgeon-General Stevenson, Colonels W. H. Henderson and R. Baker, I. M. S., and other

<sup>1</sup> Major, I. M. S.

surgeons, have also employed Keith's method in the same hospital with most encouraging results, and Colonel Henderson has published a series of a hundred and ten cases with three deaths.

Keith's original operation in its turn has in recent years undergone further modification at the hands of various operators. Surgeon-General Stevenson, it would appear, makes a slightly larger opening so as to allow of one instrument being introduced alongside another, the principle being to retain a guide all the time; while Major S. Evans prefers to make his incision somewhat further back, and thus strike the wider prostatic portion of the urethra. Both these modifications would tend theoretically to minimize what I am convinced is the reason of the comparatively slow adoption of the operation by surgeons who have not had opportunities of seeing it actually performed, namely, the risk of missing the opening in the urethra in working without a guide. However, this risk is not a great one, for Keith's original incision strikes the urethra at a point where it is easily accessible, and where the wall, surrounded by the constrictor fibers, is more likely to grasp the instrument and so prevent leakage. In my experience it is not easy to work through a small opening using say the lithotrite as a guide for the canula to follow it; and, finally, the figures quoted above speak for themselves.

In the account given below, I have adhered closely to what I understand was Keith's original procedure, for any knowledge of which I wish to express my indebtedness to Colonel Henderson. I may remark that my own experience is limited to thirteen cases, all of which recovered. Those only which call for comment were three children with large stones, necessitating prolonged manipulation and the repeated passing of instruments, and in whom the small incision did not heal, as it ordinarily does, by first intention.

#### ADVANTAGES OF KEITH'S OPERATION.

A comparison may perhaps best be made with suprapubic lithotomy in adults, and lateral lithotomy in children and in both, perineal litholapaxy is usually, I would urge, very much preferable. Suprapubic lithotomy has, I think, a larger mortality, it necessitates prolonged confinement to bed, and the patient is a nuisance to himself and his attendants. Lateral lithotomy, although very successful in children, has all the disadvantages of involuntary micturition, and there is reason to believe that in some cases the sexual powers are interfered with.

In Keith's operation there is usually no shock, micturition is voluntary, the sexual apparatus is not injured, and the period of convalescence is usually not much longer than that of ordinary litholapaxy. I personally make a practice of keeping cases in for five to seven days, but often, after twenty-four hours, healing is so far advanced as to prevent any further escape of urine from the wound, and instances have frequently been noticed in which all urine escaped via the meatus from the first.

## INDICATIONS.

Various authorities recommend perineal litholapaxy under some or all of the following conditions:

- (1) A large or very hard stone necessitating the use of a lithotrite which will not pass easily by the natural route.
- (2) Stricture, in conjunction with a large or hard stone, or perhaps with any stone.
- (3) A difficult or narrow urethra.
- (4) Imperfect equipment—the absence of the smaller sizes of lithotrite.
- (5) Cases in which litholapaxy has been commenced in the ordinary way, but can not be completed satisfactorily owing to swelling of the urethra and deposit of debris.

## THE OPERATION.

Perineal litholapaxy may thus be performed: The patient is placed in the lithotomy position, and the thighs held so that the parts are as symmetrical as possible. A curved staff with a median groove is introduced into the bladder and held as in lithotomy, but neither drawn up beneath the pubes nor depressed. The scrotum is allowed to hang down in the natural position, and neither the operator nor the assistant steadies the skin.

A very small incision, or stab, is now made with the point of a tenotomy knife or double-edge scalpel, in children about one inch, in adults one and a half inches in front of the anus, through the median raphe in the direction of the staff; the groove is entered and the urethra incised for one-eighth inch or more and the knife withdrawn, slightly enlarging the superficial part of the incision as it emerges. The point of an ordinary director, which should not be too blunt, is inserted through the wound into the groove of the staff, and passed into the bladder; the staff is withdrawn, and graduated female sounds or Hegar's dilators introduced up to the required size. Some operators do not pass the dilators so far as the bladder, but there is at all events no harm in doing so.

Dilation is proceeded with slowly, and each instrument is left in position some little time; when the required aperture has been attained the director is withdrawn, leaving a circular, gaping orifice into the urethra. The appropriate size of evacuating catheter is now passed, and the bladder injected, and the lithotrite should follow without difficulty.

If preferred, the director can be guided into the groove of the staff along the knife, before the latter is withdrawn. Both cannula and lithotrite are entered point downwards, and carried into the bladder by the usual rotatory movement. The operation is completed in the same way as an ordinary litholapaxy, and as a rule there is no difficulty in retaining fluid in the bladder; if leakage should occur at the margins of the wound it is easy to compress them against the instrument.

In order to avoid a valvular aperture (which renders the introduction of instruments difficult) it is most important that the skin should not be displaced when making the incision. Also, it is better to enter the knife too far forward than too near the anus; in the latter case the instruments enter the urethra at an acute angle instead of vertically, and are much more likely to slip past the opening, and there is the added difficulty of working in a deeper wound. The chief danger of the operation lies in the lithotrite or cannula missing the urethral

opening, and passing upwards between the bladder and the rectum; the possibility of a small median wound of the bulb, especially in children, need not give rise to anxiety, and so far as I am aware, no cases of troublesome hæmorrhage have been recorded.

It is worthy of note that, contrary to what the anatomical text-books would lead one to expect, the most difficult part of a child's urethra, after the meatus, is often well in front of the membranous portion, so that an incision in the situation recommended almost always enables instruments of reasonable size to be passed.

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## A CLINICAL STUDY OF HOOKWORM INFECTION IN THE PHILIPPINES.<sup>1</sup>

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The greater part of the work which has been done in relation to infections with hookworm has been statistical. Thus the publications of Garrison,<sup>(1)</sup> Rissler and Gomez,<sup>(2)</sup> Bowman,<sup>(3)</sup> and Willets<sup>(4)</sup> have established the varying percentages of infection in different parts of the Philippine Islands.

The investigation which is the subject of this paper was undertaken mainly to determine the effect of the hookworm on Filipinos and to determine whether there is any immunity enjoyed by the race, comparable to that of the Negros in Porto Rico, in the southern United States, and in Africa.

### MATERIAL AND METHODS.

A series of twenty-six cases was studied clinically, and subjected to a careful examination of the blood and urine.

The clinical examination included questions of the occurrence of previous diseases which would be likely to produce anæmia, such as tuberculosis, malaria, or dysentery, and queries as to present complaints. A close examination of the conjunctiva was also made because by this means the best evidence of pallor in dark-skinned people can be attained, and evidence was secured as to the presence of diseases of the lungs, heart, liver, spleen, stomach, and skin that are likely to produce eosinophilia.

The blood was examined for hæmoglobin by the Tallquist method and the erythrocytes and leucocytes estimated quantitatively. Wright's stain was used in the differential count of the leucocytes, from 300 to 800 leucocytes being counted in each case and care taken to examine the edges as well as the center of the smear.

The urine was tested for albumin by means of the heat acetic acid

<sup>1</sup>Read at the Eighth Annual Meeting of the Philippine Islands Medical Association, February 24, 1911.

and nitric acid methods, because the Anæmia Commission of Porto Rico<sup>(5)</sup> found that in many cases of hookworm infection albumin is present in the urine.

In a few cases the hookworms were collected and counted. It has been my procedure to collect the stools in every case. The patients were directed to pass all the stools in a vessel for twenty-four hours following the last purgative in the treatment, but considerable difficulty was experienced in making them comply with the instructions. Inasmuch as some worms may still be passed later than twenty-four hours after treatment, the number which I obtained may not represent the total number of parasites in every case, but the error can not be very great, as the number of hookworms recovered bears a very close relationship to the number of eggs found in a cover-glass preparation; it usually being about one to three.

Ten cases without hookworms but with other intestinal parasites were selected for study as controls.

#### DISCUSSION OF FINDINGS.

As is shown in the table, five cases out of twenty-six complained of a certain amount of pain in the stomach. The other symptoms, such as emaciation, a feeling of dizziness, pain in the joints, difficulty in urination, a sensation of oppression on the chest, tympanitis, neuralgic intercostal pains, or debility, can be attributed to other diseases such as malaria, tuberculosis, dengue fever, cystitis, and nephritis.

The vague pains in the stomach suggest the presence of hookworms, either alone or associated with other intestinal parasites, as their removal is followed by immediate relief. Pain in the gastric region as a symptom accompanying hookworm infection has been frequently observed by Doctor Rissler and me in our work in Rizal and Cavite Provinces and the Cagayan Valley. One particular instance was that of our own assistant in Las Piñas, Rizal, who complained of poor appetite and vague abdominal pains, and who was promptly relieved on the expulsion of hookworms. The occurrence of vague digestive and abdominal symptoms is also mentioned by Bass<sup>(7)</sup> in connection with mild infections with hookworm in the southern United States. The reference of the pain to the stomach and abdominal region may be explained by the anatomic arrangement of the sympathetic innervation of the duodenum which is connected, through the solar plexus, with the remainder of the abdominal organs, and particularly with the stomach.

As compared with the control cases, eosinophilia is generally present in the patients harboring hookworms. Five out of 10, or 50 per cent, of the control cases gave an eosinophile count above 4 per cent. In patients infected with hookworm, 20 out of 26, or 76 per cent, had eosinophiles above 4 per cent. Only 3 of the controls had over 5 per

cent, whereas in the hookworm series, this figure was reached by 20 out of 26 of the cases. No control shows 13 per cent or above, whereas 9 (or 34 per cent) of the cases harboring hookworms gave an eosinophile count of 13 per cent or above. The lowest count in the control cases was 0.3 per cent, and the highest 12.80, whereas in the others the lowest was 0.3 per cent and the highest 21.9. It is to be noted in the control series that individuals with *Trichuris* or *Ascaris*, or both together, hardly show any deviation from normal (0.5 to 4.00 per cent, Cabot), those having high eosinophile counts harbored amœbæ or *Tænia*. Chamberlain<sup>(6)</sup> in his work on light infection with uncinaria among southern-bred white soldiers found eosinophilia to be present in the majority of cases, the lowest count being 1 per cent and the highest 26.

The percentage of hæmoglobin in the control series varied from 80 to 95. In the cases infected with hookworms, the percentage was from 75 to 95. The count of the red and white cells does not show any marked difference between the two series; the lowest for red cells in the hookworm cases is 4,000,000 per cubic centimeter whereas in the control cases it was 4,500,000.

In two instances (3 and 12), albumin was found in the urine but this occurrence can be attributed to nephritis which was independent of the hookworm infection.

The number of hookworms recovered varied from 1 to 20, this small number corresponding to the paucity of eggs found in the microscopic preparations.

One case has been followed closely:

Case 17.—N. S., age 23, from Gerona, Tarlac. Patient previously was a clerk. Examination of the faeces, April 13, 1910, ova of *Ascaris*, *Trichuris* and hookworm were found.

*Previous diseases.*—No tuberculosis, no malaria.

*Present complaint.*—The only complaint is fleeting pains in the gastric region, about one and one-half inches to the left of the median line at the level of the costal border. This pain existed for more than three years and occurs especially in the morning when the patient's feet are bare and cold. The pain is dull and when it occurs there is simultaneously the appearance of thin watery saliva. This condition lasts from one to three days and is repeated several times a month. It has no connection with the patient's food.

*Physical examination.*—The conjunctiva are of good color, the tongue not coated, plantar surface not fissured. No murmur in heart, slight accentuation of the pulmonic second sound.

*Blood examination.*—Hæmoglobin 85 per cent, erythrocytes 5,580,000, leucocytes 6,000, polymorphonuclears 26 per cent, small mononuclears 35 per cent, large mononuclears 9 per cent, eosinophiles 20 per cent.

Two weeks after treatment the patient was interrogated concerning his pain and he said it had entirely disappeared. A month later leucocytes were examined with the following results: Polymorphonuclears 43.4 per cent, small mononuclears 36.2 per cent, large mononuclears 6.1

per cent, eosinophiles 14.1 per cent. The faeces were negative for ova of the hookworm.

The eosinophilia is possibly due to a toxin secreted by the worm. According to Ashford and King<sup>(8)</sup> this was isolated by Lussano by evaporating at a temperature of 60° to 70° the urine of a patient infected with hookworms until it became sirupy, then extracting with absolute alcohol and dissolving the extract in distilled water. He made subcutaneous injections of this supposed toxin into rabbits continuously for eight days, causing a diminution in the number of red cells, poikilocytosis and rapid formation of fibrin, all of which symptoms disappeared upon the cessation of the injections. The parasites were then expelled from the patient and a similar preparation from the urine afterwards had no effect.

Bohland<sup>(9)</sup> also believed a breaking down of the body albumin to occur, due to a poison.

The persistence of eosinophilia after the removal of the worms is explained by Leichtenstern<sup>2</sup> as a result of the hypertrophy of that portion of the bone marrow concerned in the production of eosinophiles.

The comparative absence of clinical symptoms in hookworm infections in the Philippines probably does not mean the presence of racial immunity among the Filipinos, as the infecting organisms are few. According to Thornhill,<sup>3</sup> there must at least be 500 present for from six months to one year, in order to produce such symptoms, and other patients may develop anæmia and debility as a result of only from 100 to 300 parasites.

In Porto Rico, where the disease is evident clinically, Ashford and King<sup>(12)</sup> counted the number of hookworms expelled from twenty-two patients with the following results: In 9 cases there were less than 300 worms, in 8 cases between 300 and 1,000, in 3 cases between 1,000 and 2,000, in 1 case 2,749 and in another 4,397 hookworms. Therefore, the disease in the Philippines corresponds to the light type of Stiles,<sup>(13)</sup> in which the patients show ova in the stools, but do not exhibit any, or sufficiently marked, symptoms to attract especial attention.

#### CONCLUSIONS.

1. The most frequent and only subjective symptoms in these cases of uncinariasis occurring alone or in association with other intestinal parasites were vague abdominal pains and loss of appetite.

2. Eosinophilia was found in a majority of cases, the lowest eosinophile count being 0.3 per cent, the highest 21.90 per cent.

3. Hookworm infection among the Filipinos corresponds to the light type of Stiles, that is, patients have the ova of hookworms in their stools, but no symptoms.

<sup>2</sup> Cited by Boycott and Haldane.<sup>(10)</sup>

<sup>3</sup> Cited by Scheube.<sup>(11)</sup>

4. The absence of all clinical manifestations or their insignificant characters among Filipinos infected with hookworms can not be attributed to a racial immunity, as the number of the infecting hookworm organisms in each instance is small.

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TABLE I.—Cases of

No. of case.	Date.	Prison number.	Age.	Previous residence.	Previous employment.	Examination of feces.	Previous diseases.	Present complaint.
1	1910. Mar. 7	8356	21	-----	Scout soldier.	Hookworm, <i>Trichuris</i> .	Negative ----	None -----
2	Mar. 7	18592	16	-----	Messenger.	do -----	do -----	do -----
3	Mar. 8	7979	40	Naguilian, Union.	Laborer in rice and tobacco fields.	do -----	Rheumatism.	Frequent epigastric pain.
4	Mar. 12	-----	28	Manila -----	Employee in the prison.	Hookworm, <i>Ascaris</i> , <i>Trichuris</i> .	Cough -----	Emaciation ----
5	Mar. 14	7994	24	do -----	Clerk -----	do -----	Negative ----	Vertigo for about a year.
6	Mar. 14	8376	35	-----	Laborer in rice paddies.	do -----	Malaria two years ago.	None -----
7	Mar. 15	8001	18	-----	do -----	Hookworm	Negative	do -----
8	Mar. 15	7995	21	-----	Laborer	do -----	do -----	do -----
9	Mar. 15	8003	17	-----	Laborer on abaca.	do -----	do -----	do -----
10	Mar. 29	18841	20	Luzuriaga, Occidental Negros.	do -----	Hookworm, <i>Ascaris</i> .	Indefinite fever.	Pain in joints but no fever.
11	Mar. 29	8410	23	Malolos, Bulacan.	Laborer in rice paddies.	Hookworm	Negative ----	None -----
12	Mar. 29	8028	56	Indang, Camarines.	do -----	do -----	do -----	Coughs; does not urinate freely; pain in pubic region; breath short when tired.
13	Mar. 29	8407	20	Calumpit, Bulacan.	do -----	do -----	Rheumatism.	None -----
14	Mar. 29	8408	18	do -----	do -----	Hookworm, <i>Ascaris</i> .	do -----	Pain in the epigastrium frequently.

hookworm infection.

Physical examination.	Hamoglobin per cent.	Examination of the blood.							Albumin in urine.	Number of hookworms recovered.
		Erythrocytes.	Leucocytes.	Polymorpho-nuclears.	Mononuclears.		Eosinophiles.	Basophiles.		
					Small.	Large.				
Negative -----	85			47	28	6	18	0.4	Negative.	15
Eczema of nates, months' duration.	75			67	16	6	9		do	
Negative -----	80	4,000,000	7,500	57.30	18.70	4.90	19.10	0.3	Positive	
do -----	85	4,500,000	4,800	57	39	3	0.3		Negative.	
do -----	85	4,920,000	5,600	79	14	4	3		do	
do -----	90	4,480,000	4,800	60	20	11	9		do	15
do -----	85	4,540,000	9,240	54	26	7	13		do	20
Sluggish reflexes.	75	4,880,000	4,600	60	34	3	3		do	12
Negative -----	75	4,600,000	7,000	62	16	8	14		do	14
Pale conjunctiva; coated tongue; tenderness in epigastrium.	90	5,200,000	6,960	63	21	5	10		do	6
Negative -----	90	5,500,000	11,550	67	17	5	13		do	
Slightly pale conjunctiva; tongue coated; bronchial breathing.	85	4,420,000	7,000	66	25	6	3		Positive	17
Negative -----	90	5,400,000	6,600	62	26	8	3	0.3	Negative.	
Slightly pale conjunctiva.	90	5,700,000	5,940	65	28	6	2		do	

- \* Cases 1 and 2 had hookworms collected together.

TABLE I.—Cases of

No of case.	Date.	Prison number.	Age.	Previous residence.	Previous employment.	Examination of feces.	Previous diseases.	Present complaint.
15	Apr. 13	8452	25	Victoria, Gerona, Tarlac.	Laborer in rice paddies.	Hookworm.	Rheumatism.	Feeling oppression in chest at times.
16	Apr. 13	8457	27	do	Merchant.	Hookworm, <i>Ascaris</i> .	do	Occasional tympanitis.
17	Apr. 13	8456	23	do	Clerk	Hookworm, <i>Ascaris</i> , <i>Trichuris</i> .	do	Fleeting dull epigastric pains.
18	Apr. 20	6914	23	Santo Tomas, Batangas.	Merchant.	Hookworm, <i>Ascaris</i> , <i>Ambur</i> , <i>Trichuris</i> .	do	Pain in abdomen about umbilical region occasionally; no appetite.
19	Apr. 26	8073	20	Caloocan, Rizal.		Hookworm, <i>Ascaris</i> , <i>Trichuris</i> .	do	Neuralgic intercostal, and cephalic pains.
20	Apr. 27	19102	21	Bautista, Pangasinan.	Mechanic	do	Cough; pain in chest.	None
21	Apr. 28	12112	18	Manila	Messenger.	Hookworm.	Negative	Vertigo.
22	Apr. 88	19110	22	Luna, Union.	Laborer in rice paddies.	do	Malarial fever.	None
23	May 12	8109	26	Sinay, Ilocos Sur.	Tailor	do	Spat blood	do
24	May 16	19278	24	Pandan Candatuan, Albay.	Laborer on abaca.	Hookworm, <i>Ascaris</i> , <i>Trichuris</i> .	Spat blood; dysentery, malaria.	Debility
25	May 16	8550	65	Albay, Albay.	Laborer	do	Negative	None
26	May—	19300	18	Manila	Clerk	do	Spat blood	After meals he has pain on left side of abdomen.

hookworm infection—Continued.

Physical examination.	Hemoglobin per cent.	Examination of the blood.							Albumin in urine.	Number of hookworms recovered.
		Erythrocytes.	Leucocytes.	Polymorpho-nuclears.	Mononuclears.		Eosinophiles.	Basophiles.		
					Small.	Large.				
Conjunctiva slightly pale; tongue coated; fissuring planar surface.	80	5,200,000	8,000	64	20	8	8		Negative.	1
Conjunctiva pale; tongue coated.	85	5,640,000	10,200	55	26	6	13		do	5
Slight accentuation of second pulmonic sound.	85	5,580,000	6,000	36	35	9	20		do	5
Tongue coated	90	5,200,000	6,600	58	21	7	14		do	17
Negative	90			55.43	29.89	6.52	8.42		do	5
do	90			35.35	36.67	5.53	21.90	0.50	do	
do	90			57	27	8	7	0.3	do	1
Slightly pale conjunctiva.	85			68	16	7	8	0.2	do	
Negative	90			60.35	21.11	5.19	13.33		do	
Slight dullness left apex; tenderness over epigastrium.	90			47.38	19.92	9.47	23.01	0.19	do	6
Tongue coated; conjunctiva rather pale.	90			55.77	30.48	7.24	6.59	0.18	do	10
Negative except some herpetic eruption.	95			53.79	28.51	11.91	5.23	0.54	do	

<sup>b</sup> Stool not collected.

TABLE II.—Control

No. of case.	Date	Prison number.	Age.	Previous residence.	Previous employment.	Examination of feces.	Previous diseases.	Present complaint.
1	1910. Mar. 28	18833	50	Namakpan, La Union.	Laborer on tobacco.	<i>Trichuris</i> , <i>Ascaris</i> .	Malaria a year ago.	Pain in back.
2	Mar. 28	18830	35	Lawag, Ilocos Norte.	Tailor	<i>Ascaris</i>	Opium smoker; spat blood.	None
3	Mar. 29	18834	36	Naguilian Union.	Tobacco merchant.	do	Spat blood in 1907; fever a few days ago.	Pain in chest occasionally.
4	Mar. 30	18850	27	Manila	Clerk	<i>Trichuris</i>	Negative	None
5	Mar. 30	18851	79	do	Banquero	do	do	do
6	May 13	8104	24	Bangued, Abra.	Carpenter	<i>Amoeba</i>	Pain in chest and back; bloody stools.	Bloody stools.
7	May 13	8108	27	Narvacan, Ilocos Sur.	Clerk	<i>Tenia</i>	Has had headache frequently.	Headache, pain in abdominal region and back; difficulty in urination.
8	May 16	19279	18	Guinobatan, Albay.	Laborer on abaca.	<i>Trichuris</i> , <i>Ascaris</i> , <i>Amoeba</i> .	Malaria; dysentery with mucus and blood.	Pain in epigastrium.
9	May 16	8113				<i>Ascaris</i>		
10	Mar. 28	6004				<i>Amoeba</i> , Monads.	Malaria; chronic bronchitis.	None

cases.

Physical examination.	Hæmoglobin, per cent.	Examination of the blood.							Examina- tion of urine for albumin.
		Erythro- cytes.	Leucocytes.	Polymorpho- nuclears.	Mononuclears.		Eosino- philes.	Basophiles.	
					Small.	Large.			
Negative -----	85	5,020,000	8,600	70	18	7	5		Negative.
do -----	90	5,420,000	5,600	63	32	5	0.3	0.7	Do.
do -----	95	6,000,000	6,800	63	27	9	1		Do.
do -----	90	5,200,000	10,000	69.6	20.1	6	4.2		Do.
do -----	90	4,800,000	5,400	70	20	6	4		Do.
do -----	90			52.50	27.69	7.11	12.69		Do.
do -----	90			58.75	26.04	5.64	10.54		Positive.
Tongue coated; conjunctiva slightly pale; some fissuring of the feet.	90			67.19	11.93	8.07	12.80		Negative.
do -----	95			69.49	18.64	9.33	2.3		Do.
Negative -----	80	5,500,000	8,500	67	21.00	8	4		Do.

## A CONTRIBUTION TO THE ETIOLOGY OF BERIBERI.<sup>1</sup>

By WESTON P. CHAMBERLAIN and EDWARD B. VEDDER.<sup>2</sup>

(From United States Army Board for Study of Tropical Diseases.)

In the Lancet for December 17, 1910, Fraser and Stanton report a series of experiments in which they prove that 85 per cent of the phosphorus contained in rice polishings is negligible in the prevention of polyneuritis of fowls. Their method of experiment is briefly as follows:

One hundred grams of rice polishings, containing 4.1 grams phosphorus pentoxide were extracted with 0.3 per cent hydrochloric acid solution which dissolved out 3.6 grams or 88 per cent of the phosphorus. They then added a sufficient quantity of alcohol to precipitate all the phytin contained in the solution which amounted to 3 grams or 73 per cent of the total phosphorus. The phytin was filtered out and the filtrate contained only 0.6 gram, or 15 per cent of the total phosphorus originally present in polishings.

They then fed one series of fowls on polished rice plus the phytin containing 73 per cent of the phosphorus and another series of fowls on polished rice plus the filtrate containing only 15 per cent of the phosphorus. The fowls receiving the phytin developed neuritis while those receiving the filtrate remained in good health. This proved that 85 per cent of the total phosphorus content (73 per cent contained in the phytin and 12 per cent which remained in the polishings) is unimportant in preventing polyneuritis gallinarum.

We have repeated this work done by Fraser and Stanton and are able to confirm their results. We fed three fowls on polished rice alone and three others on polished rice plus the filtrate prepared according to their method, with the result that the three fowls receiving only polished rice developed neuritis in 18, 30, and 43 days, respectively, while of the fowls fed on polished rice plus the filtrate one died at the end of 58 days of avian diphtheria without ever showing signs of neuritis, and the other two lived until the 73d day in good health, at the end of which time the experiment was concluded.

<sup>1</sup>Published with permission of the chief surgeon, Philippines Division.

<sup>2</sup>W. P. Chamberlain, major, Medical Corps, United States Army, and Edward B. Vedder, captain, Medical Corps, United States Army, members of the United States Army Board for the Study of Tropical Diseases as they Exist in the Philippine Islands.

This strikes a hard blow at the idea that the lack of phosphorus compounds is the cause of beriberi or polyneuritis gallinarum.<sup>2</sup> However, there is still a possibility that the remaining 15 per cent of phosphorus in some particular combination is the important element. We believe that our work disposes of even this possibility, and that, as a result, the idea that multiple neuritis of fowls is due to a deficiency of phosphorus compounds must be abandoned.

Our first step was to analyze this filtrate of Fraser and Stanton for inorganic constituents, and we found that it contained 0.18583 per cent magnesium phosphate and 0.01766 per cent of potassium phosphate.

In a previous paper from this laboratory Kilbourne<sup>(1)</sup> had suggested the possibility that potassium salts might bear some relation to the production of beriberi and subsequently an attempt was made by this Board<sup>(5)</sup> to settle the point by feeding one group of fowls on polished rice plus potassium chloride, another groups on polished rice plus phosphoric acid, and a third group on polished rice with the addition of both potassium chloride and phosphoric acid. These experiments were completely negative and the fowls receiving these substances developed neuritis as promptly as fowls receiving polished rice alone.

In spite of these discouraging results and the statement by Schaumann<sup>(2)</sup> that the inorganic salts can have nothing to do with the prevention of neuritis, we determined to give these salts a more thorough trial for the following reasons: First, we had demonstrated the presence of magnesium and potassium phosphate in an extract that was proved to prevent neuritis, and, therefore, even if these salts gave negative results, their elimination would further simplify the problem and would prove that a part at least of the 15 per cent of phosphorus found in the filtrate of Fraser and Stanton was not concerned in the prevention of neuritis of fowls. Second, we had observed in various analyses of rices and rice polishings that the potassium content varied in the same manner as the phosphorus content and appeared to be just as good an *index* of its neuritis-preventing or neuritis-producing power.

The following experiment was performed for this purpose. Four groups of fowls, each group consisting of four birds, were fed on polished rice. In addition, Group A received daily 0.07 gram of potassium phosphate; Group B received 0.07 gram potassium citrate; Group C received 0.07 gram potassium carbonate and Group D received 0.07 gram magnesium phosphate. These salts were administered in the dose of 0.07 gram because analyses showed that this amount was

<sup>2</sup>The view that phosphorus was the essential neuritis-preventing element has been especially advocated by Schaumann<sup>(2)</sup> but not by Fraser and Stanton who were particular in stating that the amount of phosphorus pentoxide was only an *indicator* of the neuritis-producing power<sup>(3)</sup> of the grain.

slightly greater than the quantity of potassium in five grams of polishings, which latter quantity is known to be sufficient to maintain fowls in health. In order to facilitate administration 7 grams of each of these salts except the magnesium phosphate were dissolved in 100 cubic centimeters of distilled water. The magnesium phosphate being insoluble was simply suspended in water in the proportion 7 grams to 100 cubic centimeters. One cubic centimeter of these solutions and the suspension was administered daily to each fowl with a pipette. Therefore there can be no doubt as to what each fowl actually received. We might state at this point that this method of administration has been employed in all of our experiments.

The result of this series of experiments is briefly as follows:

*Group A* (receiving potassium phosphate): One fowl developed neuritis in 22 days and one in 24 days.

*Group B* (receiving potassium citrate): One fowl developed neuritis in 22 days and one in 24 days.

*Group C* (receiving potassium carbonate): One fowl developed neuritis in 21 days and one in 23 days.

*Group D* (receiving magnesium phosphate): Two fowls developed neuritis on the 24th day.

The experiment was discontinued on the 28th day since it was considered amply demonstrated that none of these salts conferred any protection.

We may draw several conclusions from this experiment.

1. Lack of potassium as a cause of polyneuritis can probably be excluded, because we have tried four salts of this element, one of them known to be present in rice polishings and one of them being the salt of an organic acid, and all of these salts of potassium signally failed to confer protection.

2. Magnesium phosphate, a salt present in considerable quantity in the filtrate of Fraser and Stanton, is also shown to be of no value. This probably excludes the element magnesium from further consideration.

3. By a rough calculation the phosphorus contained in the magnesium and potassium phosphate of the filtrate of Fraser and Stanton which we prepared is equivalent to about one-fifth of the 15 per cent of total phosphorus remaining according to their analyses. Since we have shown that these salts are unimportant we can state at this point that 88 per cent of the total phosphorus of rice polishings is negligible. We have not given all the figures for the sake of brevity and because our results by the method which follows are so conclusive as to the unimportance of phosphorus compounds.

Fraser and Stanton<sup>(3)</sup> have shown that the neuritis-preventing principle of rice is soluble in hot alcohol and Hulshoff-Pol<sup>(4)</sup> proved that a decoction of *katjang idjo* (*Phaseolus radiatus*) has the same curative

and preventive power as the beans themselves, so that the neuritis-preventing principle of these legumes is evidently soluble in hot water. Our work, detailed below, has shown that the active neuritis-preventing principle of rice polishings is soluble in both cold alcohol and cold water.

*Experiment 1.*—One kilogram of rice polishings was mixed with about 3,000 cubic centimeters of water and allowed to macerate over night. The resultant mixture was filtered carefully after extraction had proceeded for 24 hours. Two thousand cubic centimeters of a deep yellow liquid was obtained.

Four fowls were now fed on polished rice and given daily 20 cubic centimeters of this filtrate. In this way the fowls received the substances extracted by cold water from 10 grams of polishings. After the experiment had proceeded for several weeks and the fowls appeared to remain in health the dose of the extract was reduced to 10 cubic centimeters. These four fowls all remained healthy for 70 days at the end of which period the experiment was discontinued.

The neuritis-preventing principle of rice polishings is therefore soluble in cold distilled water.

*Experiment 2.*—One kilogram of rice polishings was mixed with 3,000 cubic centimeters 95 per cent alcohol. After macerating for 24 hours, the resultant fluid was filtered, the filtrate being a perfectly clear, light green liquid. The polishings were expressed in a towel to obtain the whole of the fluid. This clear alcoholic extract was placed in a water bath on which an electric fan was turned. The alcohol was evaporated rapidly by this method without much rise in temperature. When the alcohol had all disappeared the remaining liquid was placed in a separating funnel and after standing for about half an hour, there was a clear separation into two layers. The upper and larger layer was a deep green in color and contained all the fat extracted by this method. The lower and smaller layer was brown in color and was a thick, sirupy liquid. By carefully pouring distilled water into the funnel the separation of these two layers was rendered easier, since the water lay in a third layer below the fats but above the brown liquid. The lower layer of brown sirupy liquid was then drawn off. The fat was discarded, since it has repeatedly been shown that the fat of rice polishing has nothing to do with the prevention of neuritis. The lower layer therefore contained all the substances that were dissolved out of the polishings by cold alcohol except the fats. About 25 cubic centimeters of this extracted material was obtained from 1 kilogram of polishings and was then mixed with 1,000 cubic centimeters of distilled water, when a precipitate was formed consisting of those substances, other than the fats, that are soluble in alcohol but not in water.

Four fowls were then fed on polished rice giving them a daily dose of 10 cubic centimeters of this cloudy fluid representing the substances, other than fat, dissolved by alcohol from 10 grams of polishings. Of these four fowls, one died on the 69th day, probably of avian diphtheria, without ever showing any signs of neuritis, and the other three remained in good health until the 70th day, when the experiment was discontinued.

Therefore, the neuritis-preventing principle is soluble in cold 95 per cent alcohol.

Since the neuritis-preventing principle of rice polishings is soluble in both cold water and cold alcohol, it is apparent that by combining these two solvents the resultant extract can be much simplified, because certain substances derived from the polishings are soluble in alcohol but not in water, and vice versa. This is the principle that was adopted in the following experiment.

*Experiment 3.*—The cloudy extract used in experiment 2 was filtered until a perfectly clear yellowish fluid was obtained. This fluid contained only those substances extracted from rice polishings by alcohol and soluble both in alcohol and water.

Four fowls were fed on polished rice, with a daily dose of 10 cubic centimeters of this clear extract. These four fowls lived for 70 days in good health, thereby proving that this extract is capable of preventing neuritis, since in our experience fowls fed on polished rice alone developed neuritis in about 30 days on the average.

Through the courtesy of the Bureau of Science\* the extracts used in these experiments were analyzed with the following result:

The precipitate which had not been removed from the extract used in experiment 2, but had been removed from the extract given to fowls in experiment 3, contained 0.000033 per cent phosphorus pentoxide and 0.00116 per cent nitrogen.

The clear filtrate given to fowls in experiment 3, contained 0.00165 per cent phosphorus pentoxide and 0.0406 per cent nitrogen.

It will readily be seen that the fowls in experiment 2 received the sum of the phosphorus and nitrogenous substances contained in the precipitate and filtrate. In both experiments the amount of phosphorus received was so small as to be negligible. One hundred cubic centimeters of the filtrate used in experiment 3 contained only 1.6 milligrams of phosphorus pentoxide and since the daily dose given the fowls was 10 cubic centimeters they received 0.16 milligram phosphorus pentoxide daily, whereas if they had been fed 10 grams of rice polishings they would have received from 200 to 500 milligrams of phosphorus pentoxide. The total amount of phosphorus pentoxide in rice polishings

\*We hereby desire to express our obligation to Mr. Harry D. Gibbs, Dr. A. P. West, and Mr. R. R. Williams, chemists of the Bureau of Science, who independently performed these analyses.

varies from 2 to 5 per cent so that a brief calculation will show that the extract prepared according to this method contains between  $1/1,000$  and  $1/5,000$  of the total amount of phosphorus contained in the original polishings. In other words, at least 999 parts out of each 1,000 parts of phosphorus are proven to be unimportant in the prevention of polyneuritis of fowls. It is impossible to state positively that this minute trace of phosphorus remaining in the extract is not the neuritis-preventing element, but we can at least say that it appears utterly incredible that it can be of the slightest importance. Therefore, the theory, especially advocated by Schaumann,<sup>(2)</sup> that beriberi and polyneuritis gallinarum are caused by a lack of phosphorus compounds, is strongly discredited to say the least.

However, these findings do not necessarily conflict with the statement made by Fraser and Stanton<sup>(3)</sup> and by others, including this Board, to the effect that the proportion of phosphorus pentoxide present in a rice is an *index* of its beriberi-preventing powers. Such a statement has never, so far as we are aware, been intended to convey the impression that beriberi was due to a lack of phosphorus compounds, but merely means that a rice containing phosphorus in amounts above 0.4 per cent phosphorus pentoxide necessarily has a sufficient quantity of pericarp adhering to the kernel; i. e., it is sufficiently undermilled. As shown by a former publication of the board<sup>(5)</sup> the presence of a certain percentage of potassium appears to be an equally reliable index of safety, and so in fact would be presence in a rice of a definite percentage of any substance which is found exclusively or almost exclusively in the pericarp and the aleurone layer.

The 0.0406 per cent of nitrogen contained in this extract would indicate a considerable quantity of proteid matter provided the nitrogen were present in combination with proteids. This would not seem to be the case, however, since the extract failed to give the xanthoproteic and biuret reactions and moreover we should not expect to find proteids in a fluid obtained by extracting with alcohol, but in order to prove this point we determined to test the extract by the method of dialysis.

*Experiment 4.*—The brown residue obtained from 2 kilograms of rice polishings, macerated with cold alcohol according to the method described above in experiment 2, was mixed with 300 cubic centimeters of distilled water and filtered until clear. This small bulk of water was used in order that the aqueous extract resulting might be quite concentrated. This aqueous extract, which contained only those substances soluble in cold water and cold alcohol, was then placed in a parchment bag and suspended in distilled water. This parchment was previously tested with solutions of egg albumen and sodium chloride, and it was found that the sodium chloride passed freely through the membrane while the egg albumen did not pass through at all. During the process of dialysis the apparatus was kept in the ice-box to prevent decomposition of the extract. At the end of two days, when the fluid on the outside of the bag had become a deep yellow, the diffusate was

removed and the apparatus refilled with distilled water. This process was repeated three times, and the combined fluid removed from the outside of the bag, containing all the diffusate, was brought to 1,000 cubic centimeters, while the extract remaining inside the bag, the dialysate, was diluted likewise to 1,000 cubic centimeters.

Four fowls were now fed on polished rice plus 10 cubic centimeters daily of the dialysate and four other fowls were also fed on polished rice plus 10 cubic centimeters daily of the diffusate, with the following results.

*Group 1* (four fowls receiving polished rice plus dialysate): One fowl died of inanition in 23 days. One fowl developed neuritis in 38 days, one in 42 days and one in 52 days.\*

*Group 2* (four fowls receiving rice plus diffusate): All four remained well at the end of 70 days.

Therefore, it is apparent that the neuritis-preventing substance is capable of dialyzing through a parchment membrane.

Analysis of this diffusate showed that it contained only 0.02 per cent nitrogen so that at least half of the nitrogen originally present must have been combined in some other form than proteid, because there could be no proteid present in the diffusate.

The results of this last experiment are very far-reaching in their importance. Since the neuritis-preventing substance can dialyze through a parchment membrane it must belong to the class of crystalloids, and all colloidal substances, including proteids, gums, starches, dextrans, and many other substances, may be eliminated from further consideration. Probably enzymes also can be excluded. (6)

#### CONCLUSIONS.

1. Polyneuritis gallinarum is not prevented by adding to a diet of polished rice any of the following substances; potassium phosphate, potassium citrate, potassium carbonate, potassium chloride, magnesium phosphate, phytin, phosphoric acid, or phosphoric acid combined with potassium chloride.

2. The neuritis-preventing substance in rice polishings is soluble in cold water and in cold alcohol.

3. Polyneuritis gallinarum may be prevented by means of an extract of rice polishings containing only those substances soluble in cold water

\*The rather long "incubation period" for the neuritis in this group we believe to be due to the fact that the first supply of dialysate fed to these fowls was prepared not in a bag (as described above), but in a bottle with the mouth covered with parchment. The small dialyzing surface probably rendered dialysis slow, allowing a part of the neuritis-preventing substance to remain behind and thereby delaying the onset of the disease.

and cold alcohol. This extract, so far as at present known, has the following composition:

	Per cent.
Total solids	1.34
Ash	0.03
Phosphorus pentoxide	0.00165
Nitrogen	0.0406
Sucrose	0.88

4. Multiple neuritis in fowls fed on polished rice probably is not due to lack of phosphorus compounds in the grain, as claimed by Schaumann, since out of each 1,000 parts of phosphorus contained in the rice polishings at least 999 are not concerned in preventing neuritis.

5. The neuritis-preventing substance contained in rice polishings is capable of dialysis through a parchment membrane. This excludes all colloids from consideration.

We realize that the above conclusions are based on a small series of experiments, but the results appear so conclusive and are so far-reaching in their importance that it is deemed desirable to report them at once. Further experiments are now under way to confirm the above observations and also to determine the effect on fowls of the remaining untried substances contained in this extract, including the sucrose which it will be observed constitutes much the larger part of the total solids.

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